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DIPHENYL METHYLENE DIISOCYANATE: RANGE-FINDING STUDY OF THE LUNG SENSITIZATION OF GUINEA PIGS AFTER INTRADERMAL INDUCTION WITH COVER LETTER DATED 011993

Chemical Category

DIPHENYL METHYLENE DIISOCYANATE (26447-40-5)

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MILES

86930000109

Miles Inc.
Mobay Road
Pittsburgh, PA 15205-9741
Phone: 412 777-2000

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Office of Toxic Substances Room L-100
Environmental Protection Agency
401 M Street SW
Washington, DC 20460

Attention: 8(d) Health and Safety Reporting Rule
(Notification/Reporting)

Gentlemen:

Enclosed is the English translation of a Health and Safety Study that was submitted on July 28, 1992. The pertinent information is given below.

We are submitting this study on behalf of Miles Inc., Mobay Road, Pittsburgh, Pennsylvania 15205. We are filing this Health and Safety Study to comply with the regulations codified at 40 CFR, Part 716. This submission contains no Confidential Business Information (CBI).

The information required at 40 CFR 716.30 is given below.

Chemical Name:	Diphenyl methylene diisocyanate
CAS No:	26447-40-5
Name of Study:	Range-Finding Study of the Lung Sensitization of Guinea Pigs After Intradermal Induction, Study Number T6039897
Submitting Official:	Francis J. Rattay
Title:	Manager, Regulatory Affairs
Address:	Mobay Road Pittsburgh, Pa 15205
Telephone No.:	(412) 777-7471

Sincerely,

Francis J. Rattay

Francis J. Rattay
Manager, Regulatory Affairs
(412) 777-7471

Attachment
Certified Mail No.: P 213 126 278

cc: 8(d) File 92-12-8
C. Halder*
J. Chapman - Full Report

BAYER AG
FACHBEREICH TOXIKOLOGIE
Friedrich-Ebert-Strasse 217-333
D-5600 Wuppertal 1
Federal Republic of Germany

Bayer Report No.: 21363

Date: May 13, 1992

DESMODUR VP PU 1806
(Induction and Challenge: DESMODUR VP PU 1806)

RANGE-FINDING STUDY OF THE LUNG SENSITIZATION OF GUINEA PIGS AFTER INTRADERMAL INDUCTION

by

Dr. J. Pauluhn

Study number: T6039897

GOOD LABORATORY PRACTICE STATEMENT

This study conforms to the OECD Principles of Good Laboratory Practice (GLP) [German version published in: Bundesanzeiger No. 42a (March 2, 1983) and ChemG (1990), respectively].

The study director Dr. J. Pauluhn assures, that the methods and experimental results correctly reflect the standard operation procedures and raw data.

Dr. J. Pauluhn D.A.B.T.
Fachtoxikologe DGPT
Study Director

Date: 6.12.1992

1. TABLE OF CONTENTS

2. STATEMENT THE QUALITY ASSURANCE UNIT

Study-No.: T6039897

Compound: DESMODUR VP PU 1806

The study was inspected by Quality Assurance on the dates given below. The results of the checks and the inspections are conveyed in writing to the study director and, if necessary, also to the head of the institute, or other persons affected.

Date of check/inspection	Date of issue of inspection report
Feb. 08, 1991 (study plan)	Feb. 08, 1991
Feb. 08, 1991	Feb. 13, 1991
Feb. 26, 1991	Feb. 26, 1991
Mar. 01, 1991	Mar. 01, 1991

This report was audited by QAU. All methods and data correctly reflect the methods applied and raw data. Pulmonary function data were checked at random.

Quality Assurance / GLP
Bayer AG, 5600 Wuppertal 1

Date: April 21, 1992

Responsible: Dr. H. Lehn

3. SIGNATURES

Study director:

Dr. J. Pauluhn

Director of Institute:

9.5.92

Dr. L. Machemer

4. SUMMARY

Range-finding tests were performed to determine the lung sensitization effect of DESMODUR VP PU 1806 on guinea pigs of the Pirbright-White-Dunkin-Hartley (BOR:DHPW) strain.

Experimental Procedure:
Induction: A 5% solution in kerosene was intradermally administered three times to groups consisting of 8 female guinea pigs (2 x 50 µl on days 0, 2, and 4). The vehicle (kerosene) was administered under similar conditions to 8 females serving as control animals.

After a recovery period of about 2 weeks, a DESMODUR VP PU 1806 challenge was performed (days 21-24) (mean concentration: 3.3 mg DESMODUR VP PU 1806/m³).

During and after each challenge exposure (duration: approximately 30 minutes), reactions of the immediate type were determined in all animals by measuring the respiratory rate, tidal volume, respiratory minute volume, inspiratory time, expiratory time, and peak expiratory flow. Subsequently, the respiratory rate was measured for a period of approximately 20 hours in order to quantitatively detect any delayed-type reactions. At the end of this recovery period, all guinea pigs were sacrificed. The weight of the exsanguinated lungs was determined, and the lungs and trachea were histologically examined.

Experimental Results:
Following the DESMODUR VP PU 1806 challenge, no specific respiratory reactions were observed that would be indicative of a lung sensitization potential of DESMODUR VP PU 1806. However, an increase in tidal volume and a decrease in respiratory rate, with an associated increase in inspiratory time, were observed in a few animals. These findings are considered to be causally related to an irritation of the lung periphery (triggering of the paintal reflex), since comparable effects were observed in both the control animals and those induced with DESMODUR VP PU 1806. There was no evidence of delayed respiratory reactions.

Analysis of the lung weights revealed a statistically significant increase in the absolute and relative lung weights in the DESMODUR VP PU 1806 group. However, histopathological examination of the trachea and lungs revealed no

statistically significant increase in eosinophilic granulocytes of the submucosa in the DESMODUR VP PU 1806 induction group. Accordingly, there were no toxicologically relevant reactions that could be regarded as causally related to immunological reactions.

Assessment:
This study showed that, in DESMODUR VP PU 1806-induced animals, a respirable DESMODUR VP PU 1806 aerosol does not produce any effects that are indicative of a potential for lung sensitization. Rather, these findings indicate that this test substance may be a severe irritant to the respiratory tract.

5. INTRODUCTION

In this range-finding lung sensitization study, guinea pigs of the BOR:DHPW strain were intradermally induced with DESMODUR VP PU 1806. After a recovery period of a minimum of 2 weeks, during which the animals were not exposed, a challenge exposure (about 30 minutes) using the hapten (DESMODUR VP PU 1806) was performed (3rd week after induction).

This range-finding study was performed in order to estimate the potential for lung sensitization following intradermal induction and an inhalation challenge. Our own experience with this test system, as well as recently published articles (BOTHAM et al., 1989; PAULUHN and EBEN, 1991), confirm that considerably higher anti-IgG1 antibody titers are produced after intradermal induction than after induction by inhalation. Accordingly, it is possible using intradermal induction to estimate the lung sensitization potential by means of a range-finding test to determine potential irritation. However, quantitative claims cannot be made using this test system. If the latter objective is to be accomplished, induction by inhalation is necessary.

This study was performed at the times indicated below at the Institute of Toxicology/Agriculture, Fachbereich Toxikologie, BAYER AG, Friedrich-Ebert-Straße 217-333, 5600 Wuppertal-Elberfeld, Federal Republic of Germany.

Study No.: T6039897

Induction Phase:	February 4, 1991 - February 8, 1991
Challenge:	February 25, 1991 - February 28, 1991
Necropsy:	March 1, 1991

Hapten: DESMODUR VP PU 1806, designated as "MDI" in the report.

6. RESPONSIBILITIES

Director of the Institute of Toxicology/Agriculture: ..... Dr. L. Machemer

Section Manager: ..... Dr. J. Pauluhn

Study Director: ..... Dr. J. Pauluhn

Biometrics/Software Development: ..... Dr. J. Pauluhn

Analysis/Inhalation: ..... Dr. W. Rüngeler

Test Substance Preparation: ..... Dr. Pilger

Test Substance Analysis (Identity, Stability): ..... Dr. Kausler

Monitoring of the Feed Specifications: ..... Dr. G. Meister

Conditioning and Purification of the Air: ..... Dipl.-Ing. G. Strietholt

Climate Control Technology: ..... Dipl.-Ing. G. Strietholt

Archiving of the Study Data: ..... Dr. E.A. Löbbecke

Necropsy: ..... Dr. E. Sander

Histopathology: ..... Prof. Dr. U. Mohr*

Quality Assurance: ..... Dr. H. Lehn

Quality Assurance/Inspections: ..... Dr. H.-P. Schulz

Quality Assurance/Report Audit: ..... W. Baum

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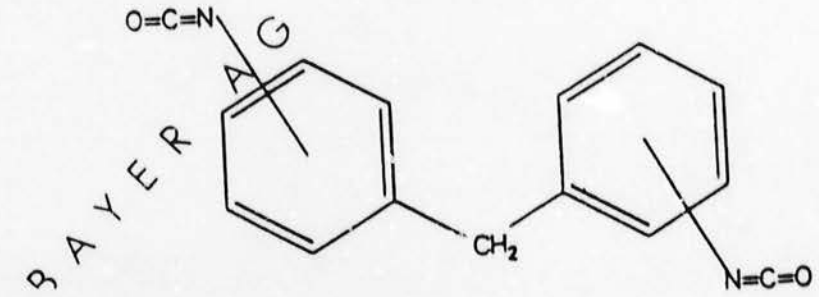
* Hochschule Hannover

7. MATERIALS AND METHODS

7.1 Test Substance Sample

Test Substance:	DESMODUR VP PU 1806
Synonyms:	Diphenylmethanediisocyanate-4,4'; 4,4'-Diphenylmethanediisocyanate; Benzene, 1,1'-methylenebis(isocyanato)-; MDI-isomer mixture
Composition:	2,2'-MDI 0.20% 2,4'-MDI 51.20% 4,4'-MDI 48.30%
Batch No.:	001326 F 072
Sample No.:	180532/90
Manufactured by:	BAYER AG, Leverkusen, Germany
Date manufactured:	February 14, 1990
Stability:	assured for the duration of the study
Storage:	room temperature / exclusion of light (under N_2)
Use:	chemical
Appearance:	red-brown liquid (at room temperature)
CAS No.:	26447-40-5

Structural formula:



Empirical formula:	$C_{15}H_{10}N_2O_2$
Molecular weight:	250.3

Melting point: 12-25°C
Boiling point: starting at 230°C
Specific gravity: 1.21 g/cm³ (at 20°C)

Vapor pressure/vapor saturation concentration: see the extrapolation table below.

MDI -- Calculation of the Vapor Pressure

°C	Vapor Pressure (kPa)	Saturation Conc. (mg/m³)
10	.12590E-06	.13384E-01
20	.47638E-06	.48916E-01
30	.16511E-05	.16394
40	.52857E-05	.50809
50	.15746E-04	1.4667
60	.43930E-04	3.9693
70	.11545E-03	10.127
80	.28725E-03	24.484
90	.67971E-03	56.340
100	.15358E-02	123.89
110	.33256E-02	261.27
120	.69237E-02	530.11
130	.13900E-01	1037.8
140	.26978E-01	1965.6
150	.50748E-01	3610.0

Parameters of the Augustian Formula (Log(P) = A + B/T):

A = 8.0366
B = -4797.2
Units -- Pressure: atm, T: Kelvin (K)
Correlation coefficient (r) = -.9832

Boiling point (extrapolated) = 587.8 K = 314.6°C
Heat of vaporization = 91840.4 J/mol
DvH/Tv (Trouton's rule) = 156.2 J/(K*mol)
Molecular weight distribution number (n) = 1.70

The calculation shows that DESMODUR VP PU 1806, in its vapor phase, is obviously present as a dimer. Since this study was performed using an aerosol and the vapor pressure at room temperature is not relevant for this type of study, the vapor pressure was not given any further consideration.

The saturation vapor pressure was calculated in accordance with the laws of equilibrium thermodynamics using a FORTRAN 77 program on an HP 3000 computer.*

*Software development and validation: Dr. J. Pauluhn.

Vehicle:

Vehicle 1:	Kerosene purum
Manufactured by:	Fluka Chemikalien: No. 60710
	Analytical No.: 297632790

In previous tests to determine stability, it was shown that DESMODUR VP PU 1806 (5%) is stable in kerosene.

7.2 Experimental Animals and Conditions of Their Care

Species and Species Justification:
The study was performed using female guinea pigs, an animal species recommended for lung sensitization studies. Female guinea pigs were used, since females gain less body weight than do males. Technical difficulties had been encountered when lung function tests were performed using the larger males in whole-body plethysmographs.

Young adult, healthy outbred guinea pigs of the strain BOR:DHPW (Pirbright-White-Dunkin-Hartley), bred by WINKELMANN (in Borchen, Paderborn District, Germany) were used. BAYER AG has used animals of this strain for years in toxicological studies. Historical data regarding their physiology and spontaneous changes are available. The state of health of the breed is routinely tested by random sampling for the most important specific infective pathogens. The results of these tests are archived.

Acclimatization:
After their receipt, the animals were acclimatized to the conditions in the animal room for at least 1 week prior to the start of treatment (animals received on January 28, 1991; Receipt No. 78680).

Identification of the Animals:
The guinea pigs were identified by individual color markings and by cage ID cards.

Randomization:
Following the acclimatization period, the physical condition of all animals was examined prior to the start of the study and the guinea pigs were randomly assigned to the treatment groups (see "Statistics").

State of Health:
Only healthy animals that were free of signs were used for the study. No vaccination or treatment of the animals with antibiotics was performed either prior to receipt or during the acclimatization period or the experimental period. The females were nulliparous and nonpregnant.

Age and Body Weight:
The mean initial body weight of the animals was about 250 g. Guinea pigs of this weight bracket are about 1 to 2 months old.

Housing of the Animals:
During both the acclimatization period and the experimental period, the animals were housed conventionally in Type IV Makrolon® cages (4 guinea pigs per cage) (A. SPIEGEL and R. GÖNNERT, Zschr. Versuchstierkunde 1:38 (1961) and G. MEISTER, Zschr. Versuchstierkunde 7:144-153 (1965)). The cages, including watering bottles, were changed at least once per week.

This study was in compliance with the legal requirements for the housing of experimental animals (86/609 EC).

Bedding:
Low-dust wood shavings (Type S 8/15) were used as bedding (supplied by SSNIFF-SPEZIALDIÄTEN GmbH, D-4770 Soest, Germany). The wood shavings were randomly tested for contaminants. The analytical results provided no evidence of an effect on the study objective.

Animal Rooms:
All animals of this study were placed in one animal room. For reasons of capacity, guinea pigs from other toxicological studies were housed temporarily in the same room. Mix-ups with other animals were avoided by adequate spatial separation (different cage racks), clear cage identification, and an appropriate scheduling of the work.

Climatic Conditions:
Conditions in the animal room were adjusted as follows:

Room Temperature:	20 ± 2°C
Relative Humidity:	approximately 50%
Light/Dark Cycle:	12 hours, artificial illumination from 6:00 a.m. to 6:00 p.m. MEZ (Central European Time)
Illumination:	approximately 14 watts/m²
Air Exchange Rate:	approximately 10 times per hour

The humidity and temperature in the animal quarters were recorded continuously using a calibrated thermohygrograph.

There were occasional deviations from these conditions, e.g. as a result of the cleaning of the animal room. They had no detectable effect on the outcome of the study.

Cleaning, Disinfection, and Pest Control:
The animal room was cleaned at least once per week and disinfected with Zephirol. In so doing, contamination of the feed and contact with the animals were avoided. No pest control was performed in the animal rooms.

Diet:
The diet consisted of a fixed-formula standard diet: "Altromin® 3022 - Haltungsdiät für Meerschweinchen" [maintenance diet for guinea pigs] (manufactured by ALTROMIN GmbH, in Lage, Germany) and tap water (watering bottles). Feed and water were available *ad libitum*. The feed was placed in an automatic feeder built into the cage.

At the request of the Central Office for Experimental Animal Concerns of BAYER AG, Wuppertal 1, Germany, the nutrient composition and the contaminant content of the standard diet were checked routinely by taking random samples and analyzing them.

The tap water was of drinking water quality (Drinking Water Ordinance dated December 5, 1990, Bundesgesetzblatt [federal law gazette], Part I, page 2600). Results of the analyses of feed and water are archived at BAYER AG. These data provided no evidence of an effect on the study objective.

Water was supplied in 700-ml polycarbonate bottles (A. SPIEGEL and R. GÖNNERT, Zschr. Versuchstierkunde, 1:38 (1961) and G. MEISTER, Zschr. Versuchstierkunde, 7:144-153 (1965)).

7.3 Guidelines

The exposure-related criteria of OECD Guideline No. 403 and the corresponding EC guideline were complied with, to the extent that they are relevant for this type of study. With regard to measuring technique, general recommendations (ASTM E 981-84; ALARIE, 1973) and essential interpretation guidelines (GROSS and VOCCI, 1988) were taken into consideration.

The procedures described were based on published methods (KAROL et al., 1985; KAROL et al., 1978; DeCEAURRIZ et al., 1987; BARROW et al., 1977; BOTHAM et al., 1988; BOTHAM et al., 1989; PAULUHN et al., 1991).

Specific, internationally coordinated test guidelines for tests to determine the lung sensitization potential in the animal test system are currently not yet available.

7.4 Range-Finding Tests to Establish Concentrations

Tests were performed using an MDI aerosol to establish the range of potential sensory irritation to guinea pigs (PAULUHN, 1991). The results are summarized below.

MDI:
Starting at a concentration of about 20 mg MDI/m³, a respirable MDI aerosol (aerosol mass with an aerodynamic diameter ≤ 3 µm: 100%) induced concentration-related respiratory changes that are indicative of an irritation of the lung periphery. Animals exposed to the maximum concentration tested (38 mg/m³) exhibited severe respiratory reactions in the form of a marked increase in tidal volume and a marginal decrease in respiratory rate, which in turn was causally related to an increase in inspiratory time.

The maximum challenge concentration for tests to determine pulmonary hypersensitivity was regarded as 20 mg MDI/m³.

7.5 Study Design

Intradermal Induction

Recently published articles have described a simplified test system to investigate the potential of haptens to sensitize guinea pig lungs (BOTHAM et al., 1989; PAULUHN and EBEN, 1991). Accordingly, an intradermal induction was performed with DESMODUR VP PU 1806 (3 x intradermal administration of 2 x 50 µl of a DESMODUR VP PU 1806 solution (5%*) in kerosene); intradermal injection in the flank of the animal at the following locations: Monday (Day 0), cranial; Wednesday, thoracic; Friday, caudal. The vehicle was intradermally injected in the control animals under similar conditions.

The stability of the DESMODUR VP PU 1806 in the vehicle was analytically verified (see point 7.9). There was no evidence of instability.

After a two-week recovery period, a DESMODUR VP PU 1806 challenge was performed.

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* All concentration data given in w/v.

Group Schedule:

Induction: Days 0, 2, 4 / intradermal, DESMODUR VP PU 1806

Challenge: exposure approximately 30 minutes / Days 21-24

Day 21	control	/ approximately	3.1 mg MDI/m³
Day 23	control	/ "	3.0 "
Day 22	DESMODUR	/ "	3.0 "
Day 24	DESMODUR	/ "	4.5 "

DESMODUR = DESMODUR VP PU 1806

For technical reasons, lung function tests were possible on only 4 animals at the same time. In the corresponding tables and graphs, each group of 8 animals is divided into two subgroups, with the first 4 animals in each case designated as subgroup "a" and the last 4 animals designated as subgroup "b."

7.6 Exposure Technique

Route of Exposure:
The guinea pigs were exposed in Plexiglas exposure tubes to the DESMODUR VP PU 1806 test substance aerosol under dynamic conditions. Exposure was thus of a head-nose type.

Vehicle:
Due to its low volatility at room temperature, the test substance was studied as an aerosol. Because of the chemical reactivity of the product, no vehicle was used in the generation of the aerosol chamber atmosphere.

The condensation aerosol of DESMODUR VP PU 1806 was fed under dynamic conditions into a cylindrical inhalation chamber (BARROW et al., 1977). The dimensions of the PVC inhalation chamber were as follows: diameter = 11.5 cm, length = 25.5 cm (volume: approximately 2.6 liters). The design of the inhalation chamber is shown schematically in Figure 1.

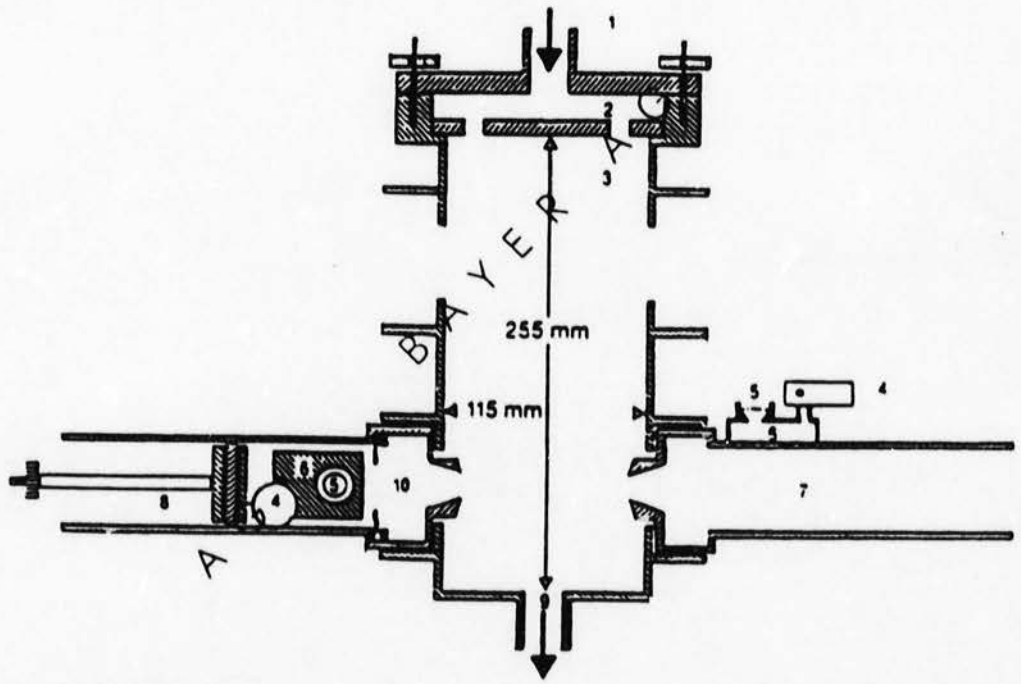
7.7 Challenge / Technical Details

Generation of the Challenge Atmosphere:
In order to ensure maximum respirability of the test substance by the test species and a maximum monodisperse distribution of the aerosol, the DESMODUR VP PU 1806 aerosol was generated as follows: The test substance was heated under a nitrogen flow of approximately 0.5 liters/minute in a temperature-controlled oil bath to approximately 130°C. The nitrogen was fed through

the test substance via a glass line. Upstream from the heating section, which was about 45 cm long (external temperature approx. 180 - 200°C), 4 to 5 liters of conditioned air were added as primary air. A temperature of approximately 150 - 170°C was determined inside the heating section by range-finding temperature measurements under these conditions. The vapor was condensed via a condensation section (approx. 115 cm long). The diameter of the glass line was approximately 2.5 cm. The aerosol generator was designed in accordance with the recommendations of RAPAPORT and WEINSTOCK (1955).

During the acclimatization and recovery periods, the animals were exposed to the above-mentioned primary air; during the challenge period, to primary air and nitrogen. The mean nominal oxygen concentration was about 18%.

Figure 1: Inhalation Chamber / DESMODUR VP PU 1806 Challenge



1. Aerosol feed
2. Deflecting plate
3. Inhalation chamber (volume: 2.6 liters)
4. Differential pressure transducer
5. Screen with perforated plate
6. Perforated cover
7. Exposure tubes (modified as whole-body plethysmograph)
8. Air-tight piston
9. Exhaust air system with flowmeter
10. Dual-membrane to separate head and thoracic region

Air Exchange Rate:
The aerosol generation conditions ensured an air exchange rate of at least 100 times per hour. Under these experimental conditions, steady state conditions are attained in a maximum of 2 minutes of operation ($t_{95\%}$ = 3 * chamber volume/ air flow; McFARLAND, 1976). Under these conditions, the ratio between supply and exhaust air was selected so that a slight positive pressure could form in the exposure system. The inhalation chambers were operated in hoods.

Conditioning of the Compressed Air:
Compressed air was generated with two BOGE compressors, Model SB 270/15/350D, connected in parallel. The fully automatic conditioning (i.e. removal of water, dust, and oil) of the compressed air was performed by means of a VIA compressed air dryer, Model A 110, connected downstream. The standard operating pressure of the compressors was 8 to 10 bar (800 to 1000 kPa). The working pressure was adjusted in each case by pressure-reducing valves.

Air Flows:
During exposure, the air flows were continuously monitored and readjusted to the nominal specifications when necessary. Air flows were generally measured against calibrated ROTA flowmeters (rotameters). The calibrated rotameters were checked against a digital flowmeter (HEWLETT PACKARD Optiflow 520) at scheduled intervals or when implausible results were obtained.

Exhaust Air:
The exhaust air was purified via a wash bottle containing a 10% aqueous NaOH solution.

7.8 Inhalation Chamber Temperature and Humidity

During the challenge period, the temperature was measured with a thermometer. Due to the chemical reactivity of the test substance, no humidity measurements were made.

The following temperature and humidity data (empirical data; PAULUHN, 1986) are regarded as representative for the challenge period:

Temperature	approx. 25°C
Relative humidity	approx. 14% (empirical data)

The inhalation chamber temperature was within the range accepted by the OECD guideline. In the DESMODUR VP PU 1806 challenge, the relative humidity was intentionally set as low as technically possible in order to minimize or prevent hydrolysis of the DESMODUR VP PU 1806 in the chamber atmosphere.

7.9 Analysis of the Chamber Atmosphere

For technical reasons, it was not possible to calculate the nominal concentration.

For absorption from the air, the DESMODUR VP PU 1806 aerosol was fed through 2 glass tubes, connected in series, that contained fiberglass wool and a glass powder layer impregnated with nitroreagent solution. This procedure produces a urea derivative that can be characterized using HPLC. The method of analytical determination has been reported separately (RÜNGELER, 1991). The air volume sampled per analysis was 50-65 liters; the mean sampling rate was about 1 liter/minute.

The air samples for the analyses were taken from the chamber atmosphere in the breathing zone of the guinea pigs, both before the start of the challenge and after the end of the challenge. For technical reasons, sampling during the challenge exposure was not possible.

All concentration data for DESMODUR VP PU 1806 are expressed in mg/m^3.

7.10 Particle Size Characterization in the Chamber Atmosphere

Samples for analysis of particle size distribution were also obtained in the immediate breathing zone of the guinea pigs.

The aerosol particle size distribution was analyzed using an Aerodynamic Particle Sizer with Laser Velocimeter (TSI-APS 3300). The APS 3300 instrument was operated with two dilution stages (TSI Model 3302). Technical details of this measurement and dilution system have been described by REMIARZ and JOHNSON (1984).

Calibration: The TSI instrument is serviced and calibrated at regular intervals by TSI, of Aachen, Germany. The method of calibration has been published (TSI, 1986). The TSI instrument is the preferred instrument because of its

high resolution capacity for smaller particles in the toxicologically relevant range (about 0.5 - 3 µm aerodynamic diameter).

The aerosol distribution parameters were calculated at the Fachbereich Toxikologie, BAYER AG, using an IBM-PC.

The calculations were based on the following principles:

TSI Laser Velocimeter:
The parameters NMAD and GSD (geometric standard deviation) that unequivocally characterize the particle number aerosol distribution were determined from the probit-transformed cumulative particle number frequency distribution (y) and the logarithmic ECD's (effective cutoff diameters) (x) of the individual measurement channels of the APS 3300 by linear regression.

The following equation was used to convert the NMAD (TSI instrument) into the MMAD:

$$\ln(MMAD) = \ln(NMAD*density) + 3(\ln(GSD))^2$$

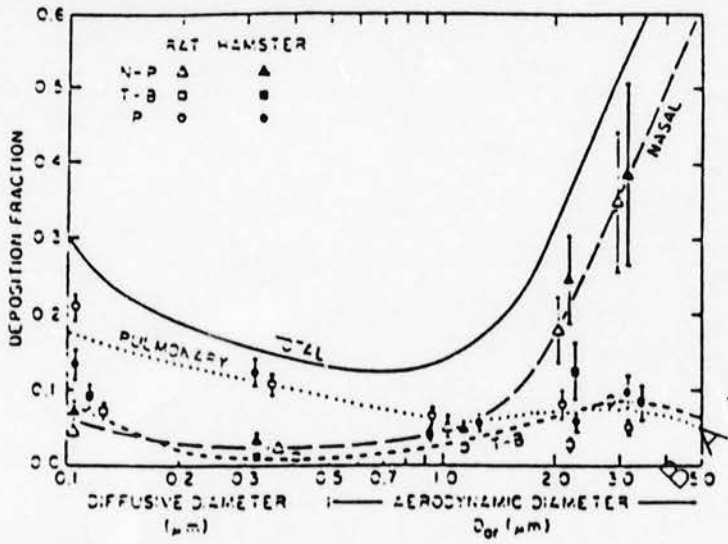
The geometric standard deviation was calculated from the regression line: percentile 84 / percentile 50.

A monomodal lognormal particle size distribution is clearly described by the MMAD or NMAD and the GSD. The proof that a monomodal particle size distribution exists is provided by the graphical comparison of the lognormal frequency distribution and the probit-transformed cumulative frequency distribution.

The following particle size distribution parameters were calculated: MMAD (Mass Median Aerodynamic Diameter), NMAD (Number Median Aerodynamic Diameter), and GSD (geometric standard deviation). The algorithms for the calculations were taken from the appropriate reference works on aerosol physics (DENNIS, 1976; MARPLE and RUBOW, 1980) and have proven to be generally applicable (PAULUHN, 1988).

The percent relative mass with an aerodynamic diameter ≤ 3 µm was regarded as the mass accessible to the alveoli. Figure 2 below shows that the existing particle size distribution (for individual data, see Appendix) is suitable to adequately expose all important potential target structures of the respiratory tract of laboratory animals (see also RAABE, 1982; SNIPES, 1989).

Figure 2: Respirability of Aerosols (according to RAABE, 1982)



Calculation of the Particle Concentration:
A Number Median Aerodynamic Diameter (NMAD) of 0.9 μm was used for this example calculation.

The DESMODUR VP PU 1806 particle density used was density = 1.21 g/ml.

Calculation of Particle Volume:

Equation: $4/3*\pi*r^3$; $r = 0.45*10^{-4}$ cm (r = NMAD/2)
$= 4/3*\pi*(0.45*10^{-4})^3$
Volume = $0.38*10^{-12}$ cm³

Calculation of Particle Mass:

Equation: volume * density; density = $1.21*10^3$ mg/cm³
$= 0.46*10^{-9}$ mg/particle
1 mg/m³ = $2.17*10^9$ particles/m³
= 2165 particles/cm³

A comparison of the vapor and aerosol atmospheres of DESMODUR VP PU 1806 (determined in combination by nitroreagent sampling) with the particle mass shows that the calculated and measured particle concentrations agree with each other within the required degree of precision and, therefore, DESMODUR VP PU 1806 is present in the form of particles (particle mass calculated: 3.9 ± 1.5 mg/m³; particle mass analytically determined: 3.3 ± 0.8 mg/m³).

7.11 Sampling

The sampling instrument was calibrated in accordance with recommendations of the ACGIH (1978; Section I "Calibration of Air Sampling Instruments").

The aerosol generating conditions were optimized to produce maximum respirability of the particles by the test species (RAABE, 1982; SNIPES, 1989) and to make it possible to disregard anisokinetic sampling errors, thus assuring a representative sampling even with different sampling geometries (ACGIH, 1978).

The tolerance limits for the radius of the sample tube (probe) were calculated as follows (ACGIH, 1978):

$$5 * \left(\frac{F * tau}{4 * \pi}\right)^{1/3} \leq r_p \leq \left(\frac{F}{g * tau * \pi}\right)^{1/2} / 5$$

F = flow = 17 to 83 cm^3/sec
tau = relaxation time = $1*10^{-4}$ sec (0.5 µm)
= $1.7*10^{-4}$ sec (7.4 µm)
g = acceleration due to gravity = 980 cm/sec^2
r_p = radius of the sample probe in cm

A calculation of the tolerance limits for the sample probe opening D_p is presented below (PAULUHN, 1988):

Isokinetic Sampling -- Tolerance Limits for Sample Probe Openings (D_p)

$F_{0.5}$	8:	0.09	<	D_p	<	20.4
	80:	0.19	<	D_p	<	64.5
$F_{7.4}$	8:	0.48	<	D_p	<	1.6
	80:	1.0	<	D_p	<	4.9

F = flow extremes (ml/sec)
D_p = inside diameter of sample probe (cm)
$F_{0.5}$ = $F_{\text{lower particle diameter (µm)}}$
$F_{7.4}$ = $F_{\text{upper particle diameter (µm)}}$

The given extremes for flow rates take into account all measuring equipment for analytical determinations. A representative sample is thus assured even under anisokinetic sampling conditions when the inside diameter of the sample probe opening is approximately $D_p = 1.3 \pm 0.3$ cm.

The openings of the sample probes used were approximately 1 cm in diameter. The instrument used for particle size analysis had a sample opening of approximately 1.5 cm. The probe openings of the sampling instruments used thus satisfy the above criteria for a representative sampling of the chamber atmosphere.

7.12 Stability of the Aerosol Chamber Atmosphere

Operation of the aerosol generating system was monitored during analytical sampling and during exposure of the animals using an RAM-1 aerosol photometer (MIE, Bedford, MA, USA). Samples were obtained continuously in the breathing zone of the guinea pigs.

This monitoring method allows for an overall observation of all toxicologically relevant inhalation chamber operating parameters (supply air, exhaust air, homogeneity of the chamber atmosphere, stability of the chamber atmosphere, operation of the aerosol generating system).

A representative result of the "Monitoring" is presented in the Appendix.

7.13 Body Weights and Recovery Period

Body weights of the guinea pigs were measured prior to the first administration, on study days 3 and 7, and weekly thereafter. The animals were also weighed on the day of necropsy.

7.14 Clinical Signs

Appearance and behavior of the individual animals were evaluated daily. The guinea pigs were also evaluated on weekends.

Evaluation in the exposure tubes is performed only if clear signs occur (e.g. convulsions, abnormal movement sequences, severe dyspnea). At the end of exposure, the animals are evaluated primarily for the following signs (at hourly intervals if necessary):

- Appearance of the visible mucosae of eyes and respiratory tract
- General condition of the rhinarium and pinna of the ear, condition of the hair coat, preening activities

- Respiration
- Circulation (to the extent assessable)
- Somatomotor activity and behavior pattern (including tremors, convulsions, hypersalivation, dyspnea, diarrhea, lethargy, sedation, and coma)
- Central nervous and autonomic signs

Since these signs can be adequately evaluated only for animals that can move freely, no specific evaluation of the guinea pigs is performed *a priori* during tube exposure.

7.15 Lung Function Tests

Reactions of the Immediate Type

The measurements were obtained from spontaneously breathing, conscious guinea pigs in head-nose exposure tubes modified as whole-body plethysmographs. The animals were acclimatized to the exposure conditions for at least 10 minutes (the animals are considered acclimatized when the respiratory rate is about 90 breaths per minutes).

The plethysmograph exposure tubes were designed to facilitate unobstructed head-nose exposure. The plethysmograph portion of the exposure tube was sealed with two latex rings and a spacer in the neck region of the animal.

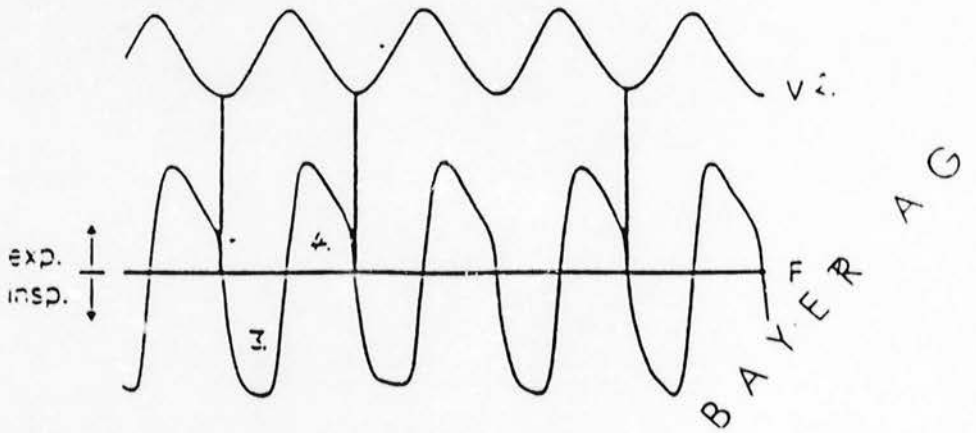
After the guinea pigs were acclimatized, the appropriate basal lung function parameters were measured for 10 minutes.

The following lung function parameters were measured:

PEF	- Peak expiratory flow	(ml/second)
TV	- Tidal volume	(ml)
RR	- Respiratory rate	(breaths/minute)
MV	- Respiratory minute volume	(ml)
IT	- Inspiratory time	(seconds)
ET	- Expiratory time	(seconds)

The measurement principle is shown in Figure 3.

Figure 3: Flow/Volume Measurement



1. Flow signal
2. Integrated flow signal (volume)
3. Inspiration
4. Expiration

The integration time was 30 seconds for all measurements.

Measurement:
The lung function testing and the calculation of the appropriate parameters were accomplished using a computer from BUXCO Electronics, CT, USA with IBM-AT coupling.

The lung function tests were performed in a flow/whole-body plethysmograph under isothermal conditions. The air flows were measured by the pressure difference produced by four 400-mesh wire screens using a differential pressure transducer (MP45 ± 2 cm H_2O, VALIDYNE, Northridge, CA, USA) attached to the wall of the plethysmograph. The operation of the plethysmograph and of the differential pressure transducers as well as the calibration of the flow integrator were checked prior to each measurement using a 2.0-ml calibration pump at a frequency of 150 strokes/minute. The dependence of the volume calibration on the frequency was checked with this reciprocating pump (in-house development of BAYER AG) at frequencies of 50, 100, 150, 200, and 250 strokes/minute. The piston displacement was also 2.0 ml. The flow resistances (screens) were adjusted so that adiabatic volume errors between 50 and 250 strokes/minutes did not exceed 10%.

The flow and volume signal for each animal was individually displayed on the CRT screen of the IBM-AT computer during the measurement. The phase and

amplitude check was recorded using an oscillograph (HONEYWELL UV recorder, Model M12 - 150A) (see Figure 3).

Evaluation:
The above-mentioned parameters were stored on a floppy disk (IBM-AT) and transferred to an HP 3000 computer using an HP ADVANCE-LINK program (Fachbereich Toxikologie, BAYER AG). The parameters of interest were averaged by this computer and printed out. The exact exposure times (air, hapten exposure, and recovery) are also presented in the tables of the Appendix.

Reactions of the Delayed Type:
Immediately after the end of the recovery period, the guinea pigs were placed in cylindrical plethysmographs (inside diameter: 12 cm, length: 23.5 cm). Bedding material (wood shavings) had been placed on the bottom of the chamber, and feed and water were available *ad libitum*.

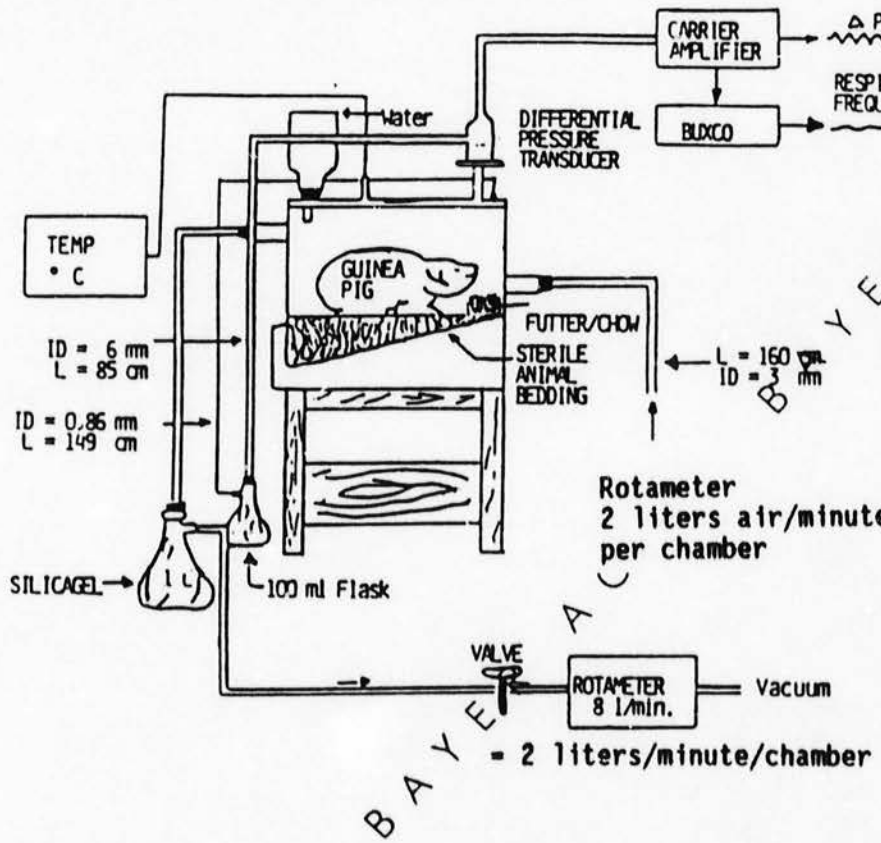
The measurement was performed using the VALIDYNE differential pressure transducer described above. The measuring period was about 20 hours. The variations in differential pressure (see Figure 4) were measured, and the respiratory rate was calculated from this data.

The integration time was 1 minute in these measurements. The data were averaged every 5 minutes for the tables and graphs in the Appendix.

The temperature in the chambers was measured with an ARUCOMP temperature probe. The chamber temperature was 21 ± 1.5°C. The chambers used had double walls, and temperature control was provided by water cooling plus a lab thermostat (JULABO UC - 5B/5).

The principle of measurement is shown in Figure 4 below.

Figure 4: Testing for Delayed Reactions (schematic)



Evaluation:
The analysis of the respiratory rate (RR) measured over a period of about 20 hours gave an average of RR = 90 with a standard deviation of s = 20 (rounded). A temporary increase in respiratory rate of 90 + 2s is regarded as a positive reaction, an increase of 90 + 3s as a severely positive reaction.

7.16 Necropsy

After the final challenge in each case, the guinea pigs were sacrificed by exsanguination via the aorta abdominalis under deep diethyl ether anesthesia and were grossly examined. All abnormal findings were recorded.

The weight of the exsanguinated lungs was determined.

7.17 Histopathology

The lungs were first fixed by instilling a 5% aqueous buffered formaldehyde solution (pressure 20 cm water for 5 minutes, trachea then ligated, and final fixation in 10% aqueous buffered formaldehyde solution). This type of fixation is considered appropriate, since a direct determination of the lung weight, a very sensitive parameter, is not possible when fixation by perfusion (via the vascular system) is used.

The fixations involving the respiratory tract were performed in accordance with the methods described by DUNGWORTH et al. (1985).

7.17.1 Histological Technique

The lungs (including trachea) were fixed in formalin and embedded in Paraplast. The sections were approximately 4-7 µm and were stained with hematoxylin and eosin (H&E). The technical sections were prepared by EPS (U.K.) Ltd., Hereford, Great Britain.

The tissues were examined histopathologically by Prof. Dr. med. U. Mohr, Department of Experimental Pathology, Hannover School of Medicine [Med. Hochschule Hannover].

7.18 Statistics / Biometrics

7.18.1 Body Weights

The means and standard deviation of the body weights were calculated. The body weight differences were statistically analyzed by means of a one-way analysis of variance (ANOVA).

7.18.2 Gross Pathological Findings

Frequent findings in the respiratory tract are statistically evaluated using the "Pairwise Fisher's Test" with preferred RxC Chi Square Test (HP 3000, Fachbereich Toxikologie, BAYER AG). The Fisher Test is performed only if there is a difference between the groups in the RxC Chi Square Test or if a frequency value < 5 is obtained. This procedure was in accordance with GAD and WEIL (1982). In calculating the one-tailed p value, a symmetrical distribution was assumed (p - one-tailed = p - two-tailed/2).

The software (Fisher Test and RxC Chi Square Test) was validated by means of data sets from the literature (GAD and WEIL, 1982; software development: Dr. J. Pauluhn). The calculations were made on an HP 3000 computer, Fachbereich Toxikologie, BAYER AG.

7.18.3 Histopathology

Histopathological findings were statistically evaluated using the "Pairwise Fisher's Test" (implemented in the P.L.A.C.E.S.-Histopathology System; Prof. Mohr, Hannover School of Medicine [Med. Hochschule Hannover]). All results are analyzed and presented as incidences, in the form of a stochastic evaluation.

Note:
As a graduated intensity, an "effect" can be correlated directly with the dose. However, certain effects do not allow an exact graduation and can therefore be regarded only as "existent" or "nonexistent." Such effects are designated as binomial effects.

The toxic effect of a substance can manifest itself in specific organ damage (target organ). In the statistical evaluation of such damage, the probability of the occurrence (incidence) and, to a lesser extent, the severity of the damage are normally regarded as a function of the administered dose (WHO, 1978). The first type of evaluation is the stochastic analysis, the second is termed nonstochastic. In histological examinations, the severity of a finding is not necessarily representative of the actual finding (peripheral cut, different planes of section). Therefore, in accordance with international recommendations, the results of histological examination are preferably analyzed and assessed in the form of a stochastic evaluation.

7.18.4 Lung Weights

Medians, arithmetic means, and standard deviation were calculated from the lung weights. The data were analyzed using an ANOVA procedure.

Both the absolute and relative lung weights are given. The relative organ weights were calculated by standardizing to 100 g body weight (individual organ weight/body weight * 100). The body weights used for these calculations were obtained in each case prior to necropsy of the animal. In preparing the graphs of these results, all means were normalized relative to the vehicle control (vehicle control = 100%). The graphs of the individual parameters show the relative standard deviation from the mean.

7.18.5 One-Way ANOVA

The one-way analysis of variance (ANOVA) can be described as follows.

In this parametric method, a normal distribution of the data is checked by comparing the median and the mean. The groups were compared at the confidence level of $(1 - \alpha) = 95\%$ ($p = 0.05$). If more than two groups were compared with each other, the test for homogeneity of the variances between the groups was performed using BOX's test. This test is preferred to BARTLETT's test when the sample size is small. If the above-mentioned F test shows that the variation within the group is larger than that between the groups, this is presented in the Appendix as "no statistical difference between the groups." If a difference is found, a pairwise post hoc comparison of the groups (one- and two-tailed) is performed using the GAMES and HOWELL modification of the TUKEY-KRAMER test for significance.

The software for the analysis of variance comes from the BCTIC Computer Code Collection, modified by PAULUHN. The software was validated by means of data sets from the literature (GAD and WEIL, 1982; BCTIC). The calculations were made on an HP 3000 computer, Fachbereich Toxikologie, BAYER AG.

7.18.6 Lung Function Tests

The extremes were calculated for the lung function parameters measured. The absolute values are presented in tables and graphs of the Appendix. All values were smoothed using a 3rd order polynomial. By this means, "peaks" which appeared briefly because of abnormal motor or respiratory activities in the plethysmograph were eliminated.

7.18.7 Particle Size Analysis

The statistical procedures used in analyzing particle size distribution were described under point 7.10.

7.18.8 Randomization

The randomization lists were generated by a computer program which uses a random number generator with varying starting conditions as the algorithm.

7.19 Presentation of the Raw Data

Data that are entered, processed, and/or stored using a computer system can be retrieved and printed out using different formatting. The number printed out and/or presented in this report is always oriented in its precision (number of decimal places) to the toxicologically relevant precision. For this reason, deviations caused by rounding off can occur between values calculated by hand and those calculated by computer. The number of decimal places "zero" does not necessarily represent the corresponding precision of the measuring and entering system.

Lung Function Tests:
The absolute values of all lung function parameters are used. The absolute values were stored on a hard disk at the same time as the measurement and were printed out. With regard to outliers, all raw data presented in the graphs were smoothed using a polynomial. Printouts of raw data (generated during the lung function test) and processed measurement data (report tables) can therefore contain slightly different values in some cases. This method is considered adequate, since evaluation of this type of test is based primarily on time profiles, not on individual values.

7.20 Archiving of the Study Documentation

All documentation pertaining to this study is stored in the archives of BAYER AG.

The prepared material for the histological examination (paraffin blocks) is archived by Prof. Dr. U. Mohr at the Hannover School of Medicine [Med. Hochschule Hannover]. The organ and tissue material and the evaluated histological sections are stored in the archives or under supervision of the archives of the Fachbereich Toxikologie, BAYER AG.

8. RESULTS

The results obtained during the DESMODUR VP PU 1806 challenge (days 21 - 24) are summarized in Table 1 below.

Table 1: Lung Function Tests - DESMODUR VP PU 1806 Challenge

Group	Induction	Anaphylaxis	Type of Respiratory Reaction Immediate	Delayed
1	Vehicle	0/ 8	5/8	(1)/8
2	DESMODUR	0/ 8	3/8	0/8

DESMODUR = DESMODUR VP PU 1806
() = marginal respiratory reactions
Anaphylaxis: Died during challenge exposure from anaphylactic shock.

#/#: 1st number: animals with positive reactions
2nd number: tested (exposed) animals

The mean challenge concentration was 3.3 ± 0.8 mg DESMODUR VP PU 1806/m³. The particle size distribution shows that, on average, the aerosol was respirable by the test species (see Appendix) (NMAD = 0.9 µm, MMAD = 1.3 µm, GSD = 1.3, particle mass ≤ 3 µm: 100%).

Signs:

Induction:
For the animals of the kerosene vehicle control and of the DESMODUR VP PU 1806 induction group, local skin reactions were observed at the injection sites: swelling, hardness, and dark discoloration of the skin with necrotic changes as well as formation of nodules between the administration sites. Animals induced with DESMODUR VP PU 1806 had reddened ears and eyelids on study days 8 and 9. In one of these animals, the injection site was bloody and moist (study days 15 and 16). Reduced activity was observed in the control animals on study days 8 - 11.

With regard to the skin reaction in the region of the administration site, there was no toxicologically relevant difference between the vehicle group and the group induced with DESMODUR VP PU 1806.

DESMODUR VP PU 1806 Challenge:
The approximately 30-minute DESMODUR VP PU 1806 challenge exposure was tolerated without signs by all animals.

Lung Function Tests:

In several guinea pigs of the vehicle control, a marked increase in tidal volume and a decrease in respiratory rate, with an associated relative increase in inspiratory time, were observed during the DESMODUR VP PU 1806 challenge. These findings are considered characteristic of an irritation of the lung periphery.

Thus, there were no specific reactions that could be regarded as causally related to pulmonary hypersensitivity. There was no evidence of delayed pulmonary reactions.

Body Weights:

The DESMODUR VP PU 1806 challenge resulted in a slight decrease in body weight in the control animals. However, there was no toxicologically relevant difference between the groups.

The body weights are presented in the Appendix.

Gross Pathological Examination:

Guinea Pigs Sacrificed at the End of the Recovery Period:
Gross pathological examination revealed comparable findings in both groups. Only Animal No. 9 (DESMODUR VP PU 1806 group) showed gross changes (lungs distended and with reddish discoloration, serous fluid in the trachea).

The individual findings are presented in the Appendix.

Lung Weights:

The absolute and relative lung weights are presented in the Appendix.

A statistically significant increase in absolute and relative lung weights was observed in animals of the DESMODUR VP PU 1806 group.

Histopathology:

The individual histopathological findings for the lungs and trachea are presented in the Appendix. The essential results are summarized in Table 3 below.

Histological examination revealed no toxicologically relevant differences between the vehicle control and the DESMODUR VP PU 1806 induction group (treatment). Peribronchial eosinophilia was observed in both groups, with the findings tending to be more severe for animals of the DESMODUR VP PU 1806 group. However, there was no statistically significant difference between the groups.

Table 3: Histopathology - Lungs and Trachea

HISTOPATHOLOGIE/HISTOPATHOLOGY

INCIDENCE OF LESIONS NUMERIC

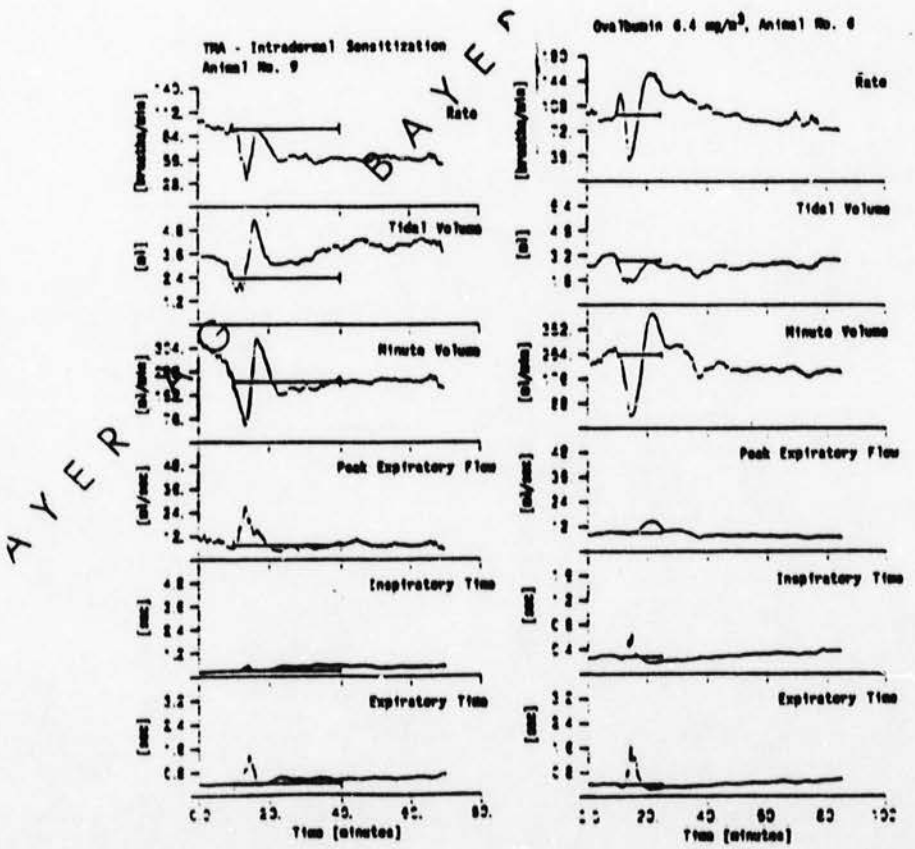
TREATMENT LESIONS	#	Control	Treatment
TRACHEA	#	(8)	(8)
Eosinophilia-slight	#	3	2
Eosinophilia-moderate/severe	#	5	6
LUNGS	#	(8)	(8)
Hyperaemia	#	3	7
Round-cell infiltration	#		
· peribronchial	#	8	8
· perivascular	#	5	6
Eosinophilia-slight	#	5	2
Eosinophilia-moderate/severe	#	2	5
Thickening of the septa	#	0	2
Marginal emphysema	#	4	8
Bronchiolar/alveolar prol.	#	8	8

(#) = number of histopathologically investigated animals

9. DISCUSSION AND ASSESSMENT

In animals induced intradermally with DESMODUR VP PU 1806, this study revealed no respiratory changes, either during or after the DESMODUR VP PU 1806 challenge, that are considered characteristic of immediate-type or delayed-type reactions. Reactions of the immediate type, as had been observed under comparable experimental conditions using trimellitic anhydride as positive control (PAULUHN, 1990; PAULUHN and EBEN, 1991), were not observed (see Figure 5). It has also been shown in tests using ovalbumin as the positive test substance (PAULUHN and EBEN, 1989) that the guinea pig strain used for these tests (Pirbright-White-Dunkin-Hartley) is suitable for lung sensitization tests, and that the test method is sufficiently sensitive quantitatively to detect small changes in spontaneous respiration.

Figure 5: Respiratory Reactions after Administration of Trimellitic Anhydride



The individual lung function data (see Appendix) show that slight respiratory reactions occurred in a few animals at the start of the challenge and at the end of the challenge. These findings could be regarded as causally related to the manipulations of the aerosol generating system performed at these times.

Analysis of the lung weight/body weight ratio revealed a statistically significant increase in lung weight in the animals of the DESMODUR VP PU 1806 group. Histological examination did not reveal any morphological correlation to the increased lung weights. Peribronchial eosinophilia was observed in both the control group and the DESMODUR VP PU 1806 induction group. However, there was no statistically significant difference between the groups.

This study, therefore, leads to the conclusion that, in guinea pigs induced with DESMODUR VP PU 1806, there were no respiratory reactions after a DESMODUR VP PU 1806 challenge that would be comparable to those obtained using ovalbumin or trimellitic anhydride as positive substance (PAULUHN and EBEN, 1991). It is possible that the increased lung weights may be considered to be causally related to a Type IV reaction.

10. KEY TO THE ABBREVIATIONS AND SYMBOLS USED IN THE TABLES

PEF	Peak expiratory flow
MV	Minute volume
TV	Tidal volume
IT	Inspiratory time
ET	Expiratory time
RR	Respiratory r[illegible]e
nomin. Konz.	Nominal concentration
mcm/µm	Micrometer
Expos.	Exposure
MMAD	Mass Me[illegible]n Aerodynamic Diameter
NMAD	Number [illegible]ian Aerodynamic Diameter
GSD	Geometric standard deviation
ECD	Effective cut-off diameter
STAND, S, Std, s	Standard deviation (σ)
MW/MEANS, x̄	Means
B.W.	Body weights
F	F test value
DF	Degrees of freedom
PROB	Probability
SS	Total sum of squares
MS	Mean squares
TREATMENT	- between the groups
ERROR	- within the groups
TOTAL	- total
Observation No.: n-nn	Body weight gain from date n to date nn

Lung Weights
- absolute in mg
- relative in mg/100 g body weight

cont./vehi	Vehicle control [induction]
treat.	DESMODUR VP PU 1806

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Principles and Methods for Evaluating the Toxicity of Chemicals Part 1, Environmental Health Criteria 6, page 26, World Health Organization, Geneva 1978.

Translation of German entries:

CHEMG
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EC Guideline 84/449
Journal of the European Community -- Legal Specifications L 251, 27, September 19, 1984.
B.2. Acute Toxicity -- Inhalation, p. 99.

EC Guideline 86/609/EC
Guideline of the Council dated November 24, 1986 on the Reconciliation of Legal and Administrative Regulations of the Member Countries for the Protection of Animals used for Studies and Other Scientific Purposes.
Journal of the European Community, Legal Specifications L 358, 29 (1986).

OECD - GLP
Publication of the German version of the OECD Principles of Good Laboratory Practice (GLP), *Bundesanzeiger*, 35, No. 42a dated March 2, 1983.

PAULUHN, J.
MDI -- Range-Finding Study to Assess Potential Irritation to Guinea Pigs; BAYER AG report undergoing Quality Assurance audit (status 1991).

PAULUHN, J. and A. EBEN
Ovalbumin -- Study of the Lung Sensitization of Guinea Pigs (Method Validation); BAYER AG Report No. 18215 dated July 26, 1989.

PAULUHN, J.
Trimellitic Anhydride -- Range-Finding Study of the Lung Sensitization of Guinea Pigs after Dermal Induction; BAYER AG Report No. 19619 dated October 15, 1990.

PAULUHN, J.
Study to Determine Temperature and Humidity Data in Inhalation Chambers; BAYER AG Report No. 15007 dated August 22, 1986.

RÜNGELER, W.
DESMODUR VP PU 1806 -- Concentration Determinations in the Chamber Atmosphere; BAYER AG Report No. 20038 dated March 4, 1991.

12. APPENDIX

Analytical Concentrations -- DESMODUR VP PU 1806 Challenge

Date (day.month.year)	Analytical Concentration (mg/m³)	
25.02.91	3.1 - 3.0	(Group 1a)
26.02.91	2.6 - 3.3	(Group 2a)
27.02.91	3.3 - 2.6	(Group 1b)
28.02.91	5.3 - 3.6	(Group 2b)
MEAN	3.35	
STD	0.86	

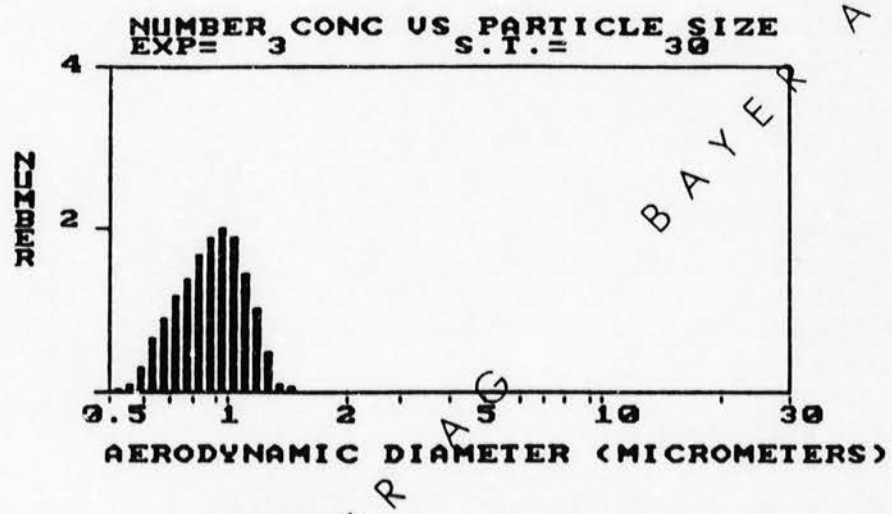
Analytical Concentrations: 1st value = concentration prior to challenge
2nd value = concentration after challenge

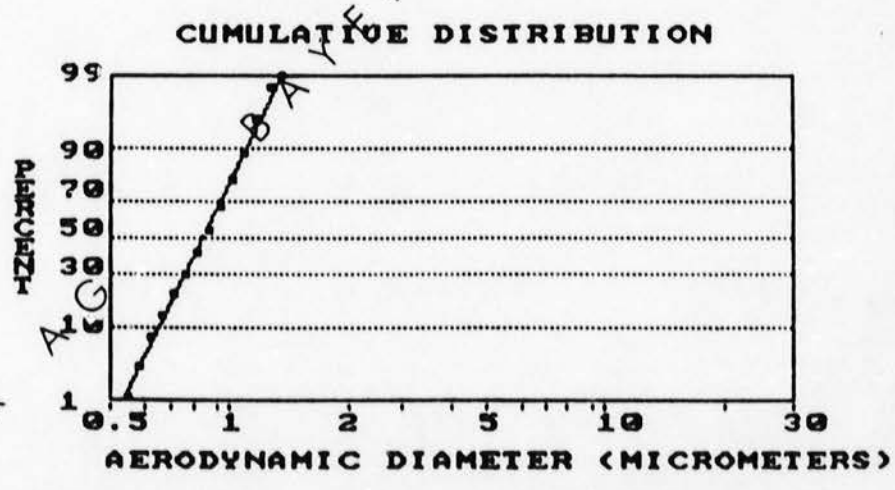
Particle Size Analysis - DESMODUR VP PU 1806 Challenge

DESMODUR VP PU 1806/T6039897 Nominal Conc. 5 mg/m³

SAMPLE # 1 DATE: 25.02.1991 SAMPLE TIME: 30 SEC DENSITY: 1.21
DIL. RATIO: 100 :1 EFFIC. CORRECT.: D100
TIME: 10:34 OPERATOR: THIE

LAST CALIBRATION: 09-20-1990 SN 152



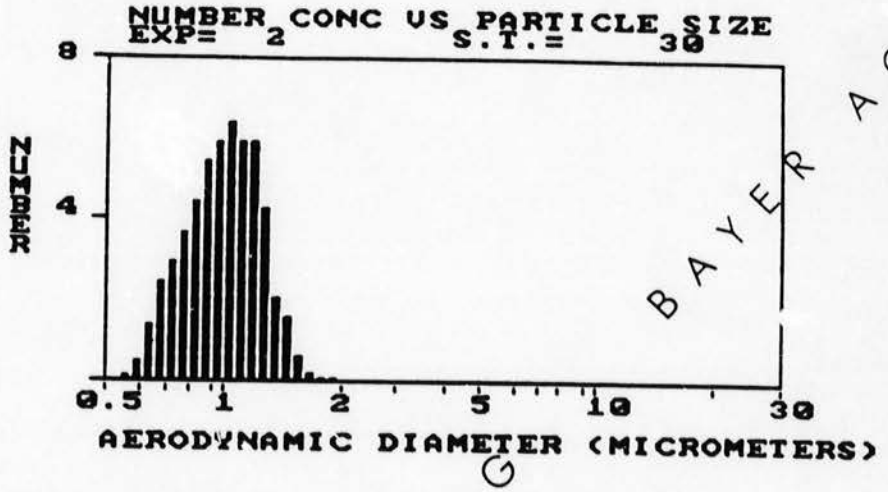


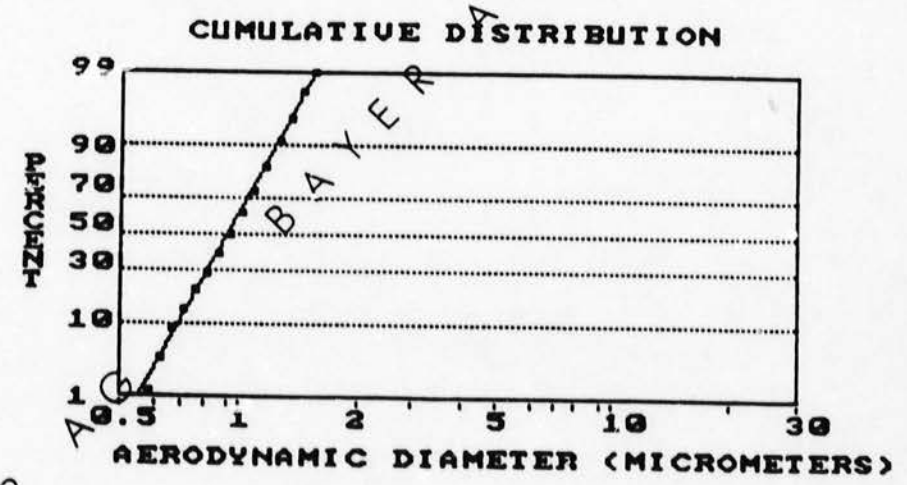
NUMBER MEDIAN DIAMETER (NMAD)	:	0.86 µm
MASS MEDIAN DIAMETER (MMAD)	:	1.18 µm
GSD	:	1.23
MASS FRACTION < 3 µm	:	100 PERCENT
PARTICLES PER cm³	:	15127.0
CONCENTRATION (COMPUTED)	:	6.1 mg/m³

Desmodur VPPU 1806/T6039897 soll Konz. 5 mg/cbm

SAMPLE # 1 DATE: 26.02.1991 SAMPLE TIME: 30 SEC DENSITY: 1.21
DIL. RATIO: 100 :1 EFFIC. CORRECT.: D100
TIME: 09:30 OPERATOR: THIE

LAST CALIBRATION: 09-20-1990 SN 152





BAYER AG

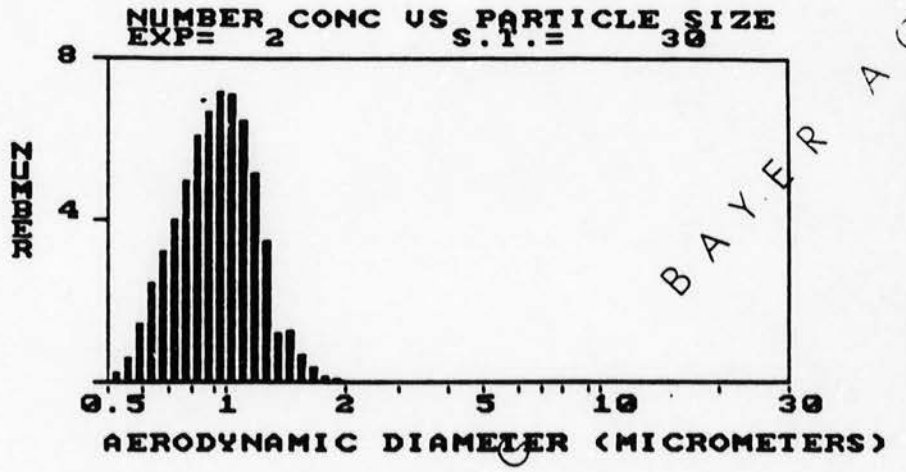
NUMBER MEDIAN DIAMETER (NMAD): 0.95 µm
MASS MEDIAN DIAMETER (MMAD): 1.34 µm
GSD : 1.26

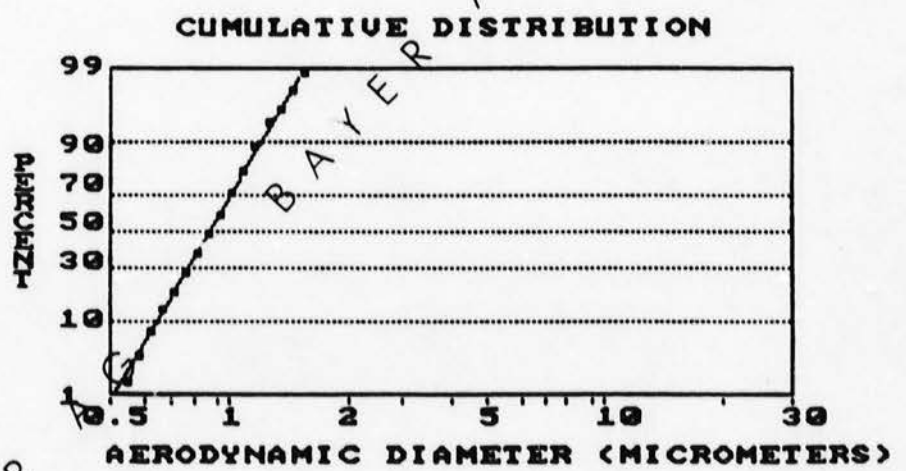
MASS FRACTION < 3 µm : 100 PERCENT
PARTICLES PER cm³ : 5394.7
CONCENTRATION (COMPUTED) : 2.9 mg/m³

Desmodur VPPU 1806/T6039897 soll Konz. 5 mg/cbm

SAMPLE # 1 DATE: 27.02.1991 SAMPLE TIME: 30 SEC DENSITY: 1.21
DIL. RATIO: 100 :1 EFFIC. CORRECT.: D100
TIME: 10:21 OPERATOR: THIE

LAST CALIBRATION: 09-20-1990 SN 152





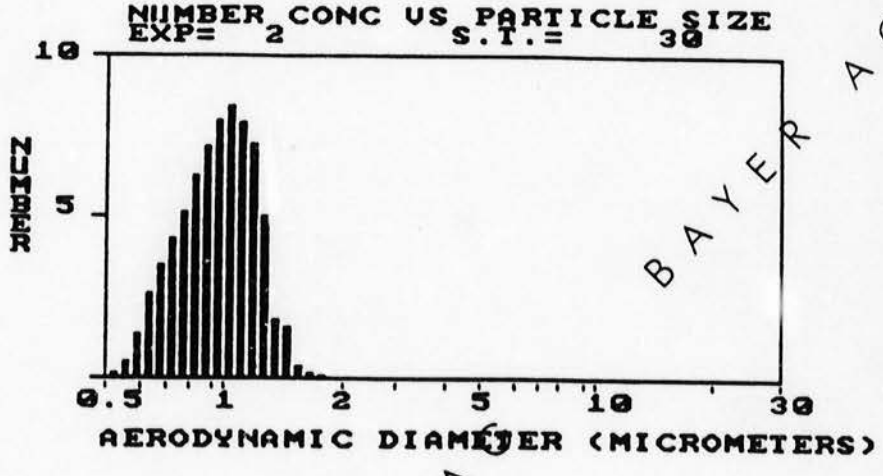
NUMBER MEDIAN DIAMETER (NMAD): 0.90 µm
MASS MEDIAN DIAMETER (MMAD): 1.31 µm
GSD : 1.28

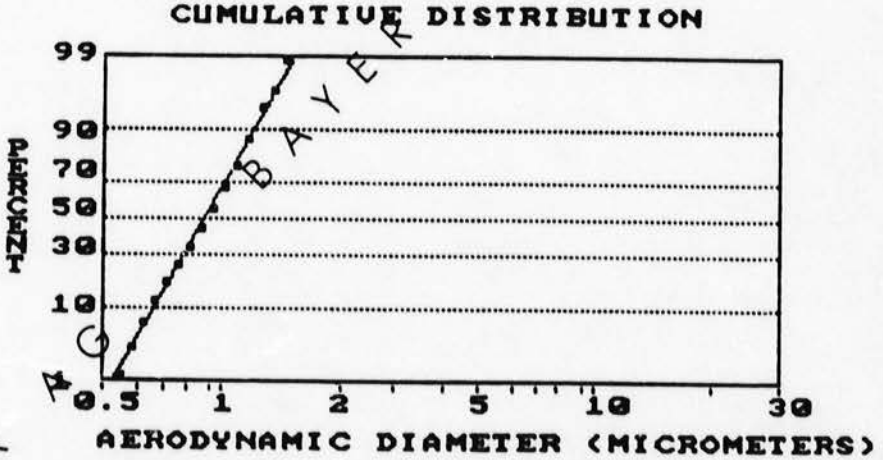
MASS FRACTION < 3 µm : 100 PERCENT
PARTICLES PER cm³ : 6286.2
CONCENTRATION (COMPUTED) : 2.9 mg/m³

Desmodur VPPU 1806/T6039897 soll Konz. 5 mg/cbm

SAMPLE # 1 DATE: 28.02.1991 SAMPLE TIME: 30 SEC DENSITY: 1.21
DIL. RATIO: 100 :1 EFFIC. CORRECT.: D100
TIME: 10:29 OPERATOR: THIE

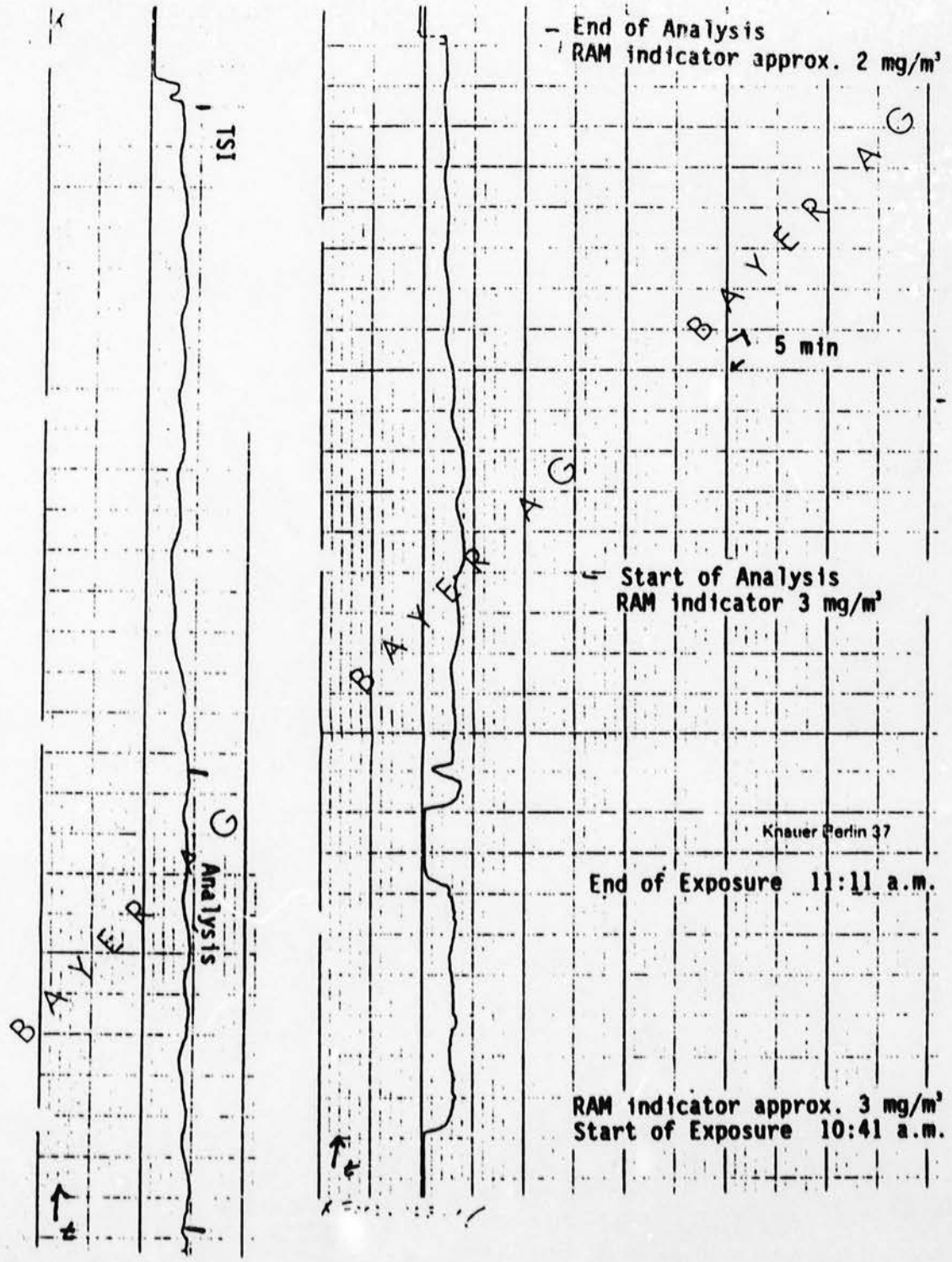
LAST CALIBRATION: 09-20-1990 SN 152





NUMBER MEDIAN DIAMETER (NMAD)	:	0.91 µm
MASS MEDIAN DIAMETER (MMAD)	:	1.30 µm
GSD	:	1.26
MASS FRACTION < 3 µm	:	100 PERCENT
PARTICLES PER cm³	:	7216.6
CONCENTRATION (COMPUTED)	:	3.5 mg/m³

Monitoring - DESMODUR VP PU 1806-Challenge



Randomization List

Randomization of the Experimental Animals

Animal Species:	Guinea pig
Date animals received:	January 28, 1991
Receipt No.:	78680
Test Substance:	DESMODUR VP PU 1806
Study No.:	T6039897
No. of animals available:	20
No. of animals required:	16
Start of study:	February 4, 1991

Treatment No.	No.
1	16
2	14
3	15
4	11
5	12
6	6
7	8
8	4
9	18
10	9
11	5
12	1
13	17
14	19
15	10
16	13

Date: January 31, 1991 Signature: [signed: Hilb]

Körpergewichte / body weights

I: Tag 0 / day 0
II: Tag 3 / day 3
III: Tag 7 / day 7
IV: Tag 14 / day 14
V: Tag 21 / day 21
VI: Tag 25 / day 25
No.: Tier-Nummer / animal number

Konzentration/concentration: control
Gruppe/group: 1 - sex: FEMALE

No.	I	II	III	IV	V	VI
1	259.0	266.0	278.0	336.0	368.0	364.0
2	225.0	222.0	230.0	266.0	314.0	316.0
3	231.0	240.0	240.0	310.0	359.0	363.0
4	243.0	250.0	269.0	319.0	356.0	370.0
5	251.0	242.0	245.0	314.0	350.0	341.0
6	267.0	261.0	296.0	343.0	381.0	383.0
7	259.0	256.0	278.0	315.0	350.0	354.0
8	260.0	255.0	273.0	327.0	377.0	374.0
MEAN	249.4	249.0	263.6	316.3	356.9	358.1
STD	15.0	14.0	22.7	23.3	20.9	21.2

Alle Gewichte in g / all weights in g

Konzentration/concentration: DESMODUR VP PU 1806-Group
Gruppe/group: 2 - sex: FEMALE

No.	I	II	III	IV	V	VI
9	260.0	276.0	293.0	337.0	393.0	394.0
10	260.0	263.0	285.0	325.0	378.0	375.0
11	267.0	279.0	294.0	330.0	385.0	390.0
12	268.0	280.0	305.0	332.0	375.0	365.0
13	229.0	238.0	252.0	295.0	344.0	336.0
14	248.0	263.0	287.0	313.0	353.0	360.0
15	254.0	265.0	276.0	326.0	384.0	361.0
16	260.0	260.0	287.0	314.0	363.0	342.0
MEAN	255.8	265.5	284.9	321.5	371.9	365.4
STD	12.6	13.6	15.7	13.6	17.0	20.6

Alle Gewichte in g / all weights in g

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR FEMALE- OBSERVATION-No.: 1- 2

Group-No.: 1 / control

7.0	-3.0	9.0	7.0	-9.0
-6.0	-3.0	-5.0		

MEDIAN= -3.0 MEAN= -.4 STD= 6.9

Group-No.: 2 / DESMODUR VP PU 1806-Group

16.0	3.0	12.0	12.0	9.0
15.0	11.0	.0		

MEDIAN= 11.5 MEAN= 9.8 STD= 5.6

NOT ENOUGH GROUPS FOR BOX'S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
1.5393	7. & 7	.2909

HOMOGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	410.1	1	410.06	10.300	.006
ERROR	557.4	14	39.813		
TOTAL	967.4	15			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST (WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	4.54	13	.0068	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	4.54	13	.0068	SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR FEMALE- OBSERVATION-No.: 2- 3

Group-No.: 1 / control

12.0	8.0	.0	19.0	3.0
35.0	22.0	18.0		

MEDIAN= 15.0 MEAN= 14.6 STD= 11.3

Group-No.: 2 / DESMODUR VP PU 1806-Group

17.0	22.0	15.0	25.0	14.0
24.0	11.0	27.0		

MEDIAN= 19.5 MEAN= 19.4 STD= 5.9

NOT ENOUGH GROUPS FOR BOX'S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
3.7204	7. & 7	.0525

HOMOGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	90.25	1	90.250	1.107	.311
ERROR	1142.	14	81.554		
TOTAL	1232.	15			

NO OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL
NO STATISTICAL DIFFERENCE BETWEEN THE GROUPS

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR FEMALE- OBSERVATION-No.: 3- 4

Group-No.: 1 / control

58.0	36.0	70.0	50.0	69.0
47.0	37.0	54.0		

MEDIAN= 52.0 MEAN= 52.6 STD= 12.9

Group-No.: 2 / DESMODUR VP PU 1806-Group

44.0	40.0	36.0	27.0	43.0
26.0	50.0	27.0		

MEDIAN= 38.0 MEAN= 36.6 STD= 9.1

NOT ENOUGH GROUPS FOR BOX´S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
1.9865	7. & 7	.1924

HOMOGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	1024.	1	1024.0	8.221	.012
ERROR	1744.	14	124.55		
TOTAL	2768.	15			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF TUKEY-KRAMER´S HONESTLY SIGNIFICANT DIFFERENCE TEST (WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	-4.05	13	.0132	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	4.05	13	.0132	SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR FEMALE- OBSERVATION-No.: 4- 5

Group-No.: 1 / control

32.0	48.0	49.0	37.0	36.0
38.0	35.0	50.0		

MEDIAN= 37.5 MEAN= 40.6 STD= 7.2

Group-No.: 2 / DESMODUR VP PU 1806-Group

56.0	53.0	55.0	43.0	49.0
40.0	58.0	49.0		

MEDIAN= 51.0 MEAN= 50.4 STD= 6.4

NOT ENOUGH GROUPS FOR BOX'S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
1.2677	7. & 7	.3807

HOMOGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	380.3	1	380.25	8.270	.012
ERROR	643.8	14	45.982		
TOTAL	1024.	15			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST (WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	4.07	14	.0122	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	4.07	14	.0122	SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR FEMALE- OBSERVATION-No.: 5- 6

Group-No.: 1 / control

-4.0	2.0	4.0	14.0	-9.0
2.0	4.0	-3.0		

MEDIAN= 2.0 MEAN= 1.3 STD= 6.9

Group-No.: 2 / DESMODUR VP PU 1806-Group

1.0	-3.0	5.0	-10.0	-8.0
7.0	-23.0	-21.0		

MEDIAN= -5.5 MEAN= -6.5 STD= 11.2

NOT ENOUGH GROUPS FOR BOX'S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
2.6707	7. & 7	.1093

HOMOGENEITY OF VARIANCES

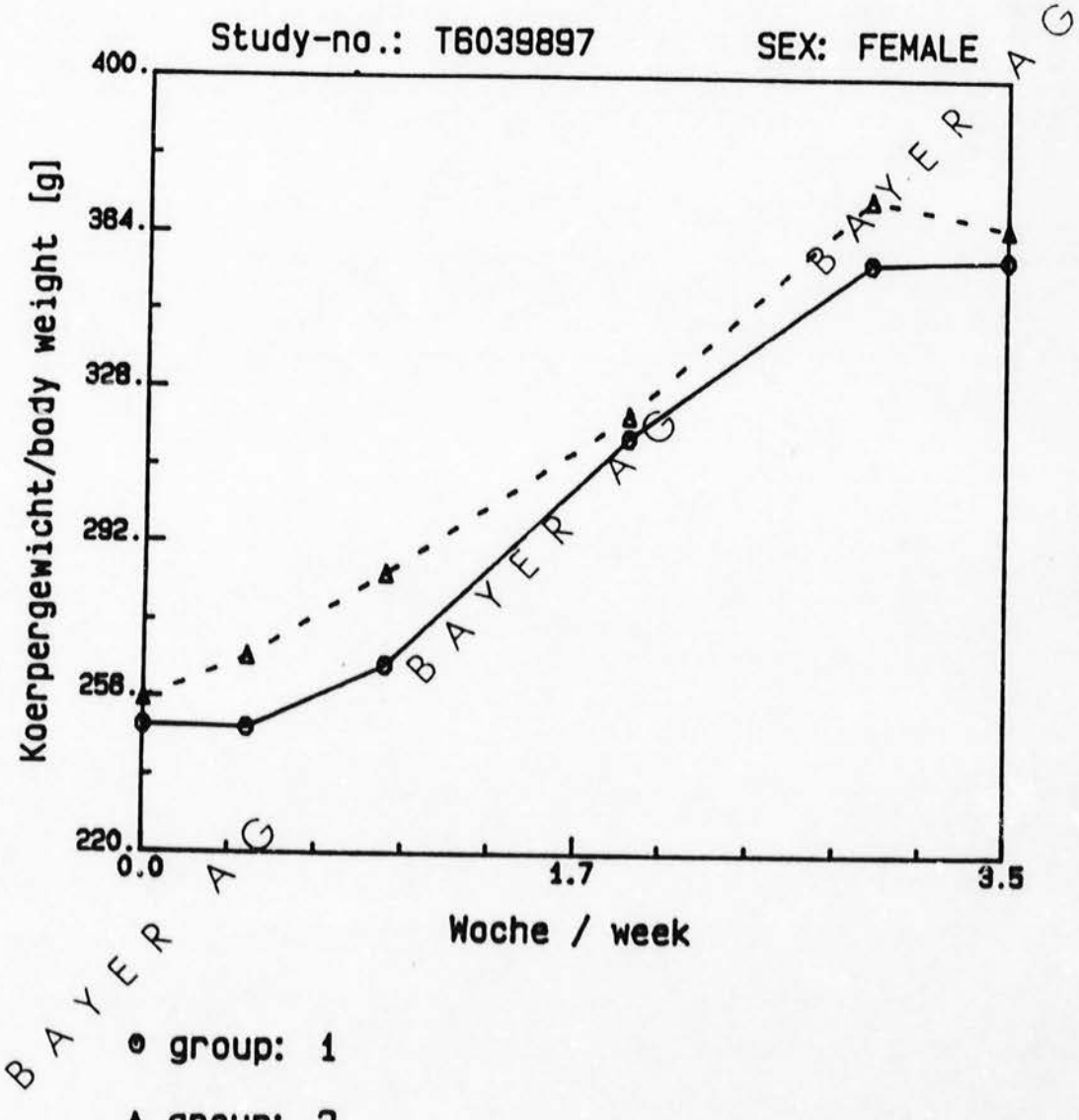
ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	240.3	1	240.25	2.781	.115
ERROR	1210.	14	86.393		
TOTAL	1450.	15			

NO OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL
NO STATISTICAL DIFFERENCE BETWEEN THE GROUPS

Body Weight Curves

DESMODUR VP PU 1806



Lung Weights

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of LUNG WEIGHT - absolute/FEMALES

Group-no.: 1 - Animal:1-8 - control
2756.000 2182.000 2675.000 2576.000 2906.000
2589.000 2527.000 2897.000
MEDIAN= 2632.000 MEAN= 2638.500 STD = 233.287

Group-no.: 2 - Animal:9-16 - DESMODUR VP PU 1806-Group
4034.000 3822.000 3201.000 3036.000 3025.000
2681.000 2795.000 2819.000
MEDIAN= 3030.500 MEAN= 3176.625 STD = 494.850

NOT ENOUGH GROUPS FOR BOX'S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
4.5026	7. & 7	.0331

HETEROGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	1.158E+06	1	1.1583E+06	7.741	.014
ERROR	2.095E+06	14	1.4963E+05		
TOTAL	3.253E+06	15			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
1. % ONE-TAILED TEST				
1 AND 2	3.93	10	.0194	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	3.93	10	.0194	SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of LUNG WEIGHT - relative to BODY WEIGHTS/FEMALES

Group-no.: 1 - Animal:1-8 - control

757.143 690.506 736.915 696.216 852.199
675.979 713.842 774.599

MEDIAN= 725.378 MEAN= 737.175 STD = 57.539

Group-no.: 2 - Animal:9-16 - DESMODUR VP PU 1806-Group

1023.858 1019.200 820.769 831.781 908.298
744.722 774.238 824.269

MEDIAN= 828.025 MEAN= 867.392 STD = 105.314

NOT ENOUGH GROUPS FOR BOX´S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
3.3501	7. & 7	.0669

HOMOGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

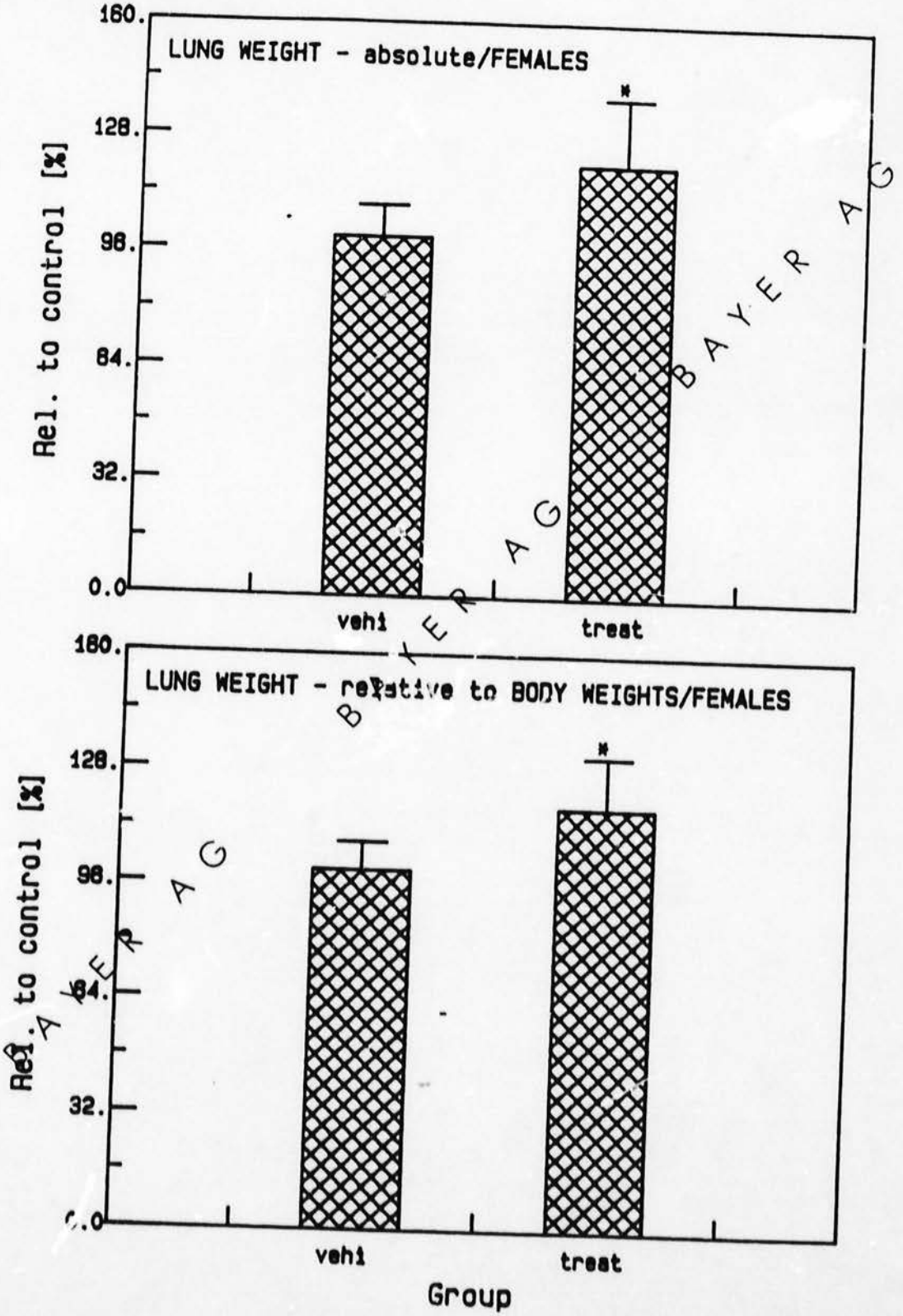
SOURCE	SS	DF	MS	F	PROB
TREATMENT	6.783E+04	1	67826.	9.419	.008
ERROR	1.008E+05	14	7200.9		
TOTAL	1.686E+05	15			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF TUKEY-KRAMER´S HONESTLY SIGNIFICANT DIFFERENCE TEST (WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	4.34	11	.0107	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	4.34	11	.0107	SIGNIFICANT

Lung Weights - Bar Graph Presentation



Body Weights - Time of Necropsy

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of BODY WEIGHTS/FEMALES

Group-no.: 1 - Animal:1-8 - control

364.000	316.000	363.000	370.000	341.000
383.000	354.000	374.000		

MEDIAN= 363.500 MEAN= 358.125 STD = 21.230

Group-no.: 2 - Animal:9-16 - DESMODUR VP PU 1806-Group

394.000	375.000	390.000	365.000	336.000
360.000	361.000	342.000		

MEDIAN= 363.000 MEAN= 365.375 STD = 20.619

NOT ENOUGH GROUPS FOR BOX'S TEST

CALCULATED F	DEG. OF FREEDOM	PROBABILITY
1.0602	7. & 7	.4704

HOMOGENEITY OF VARIANCES

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

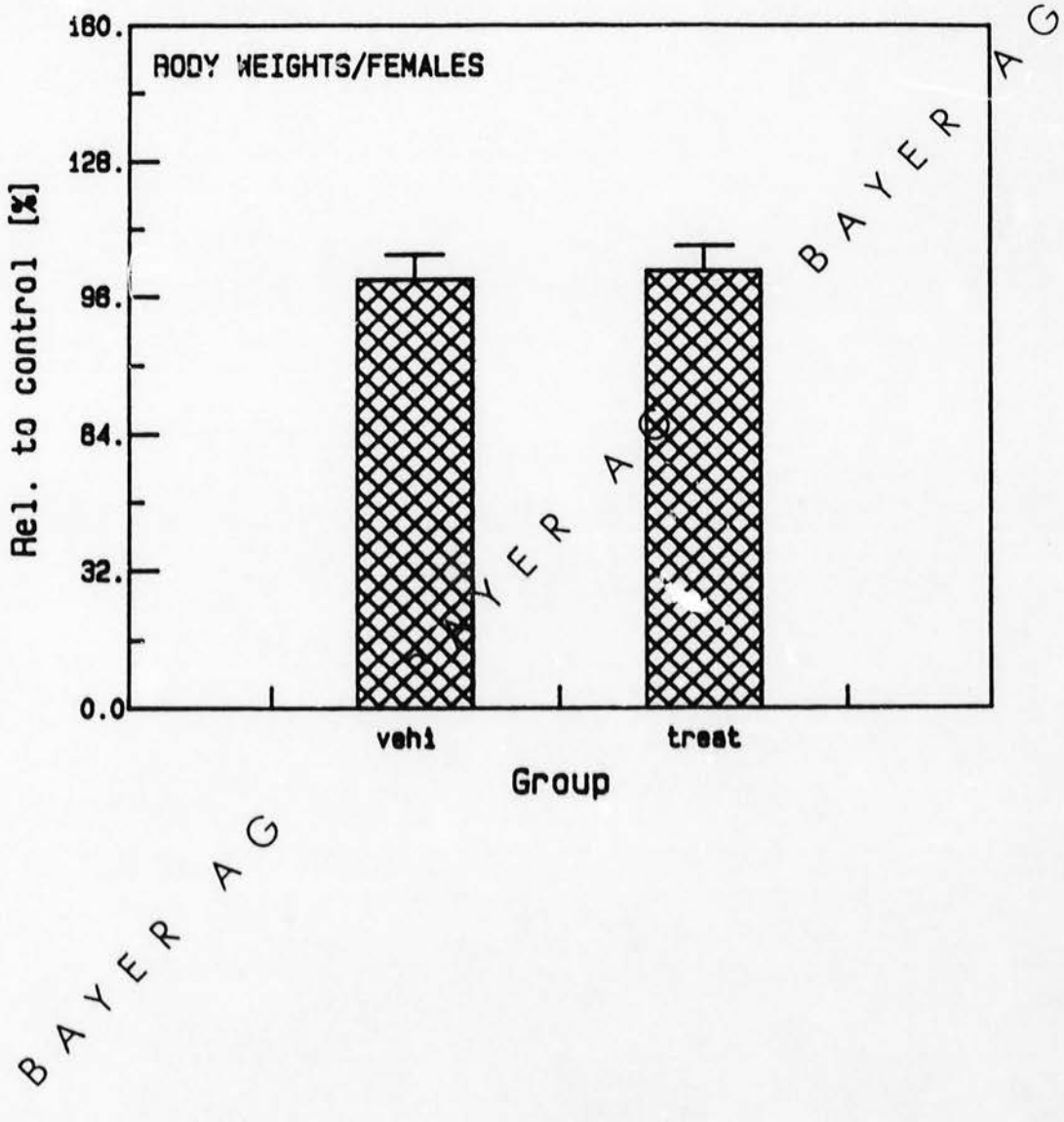
SOURCE	SS	DF	MS	F	PROB
TREATMENT	210.3	1	210.25	.480	.506
ERROR	6131.	14	437.91		
TOTAL	6341.	15			

NO OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL
NO STATISTICAL DIFFERENCE BETWEEN THE GROUPS

Body Weights - Time of Necropsy / Bar Graph Presentation

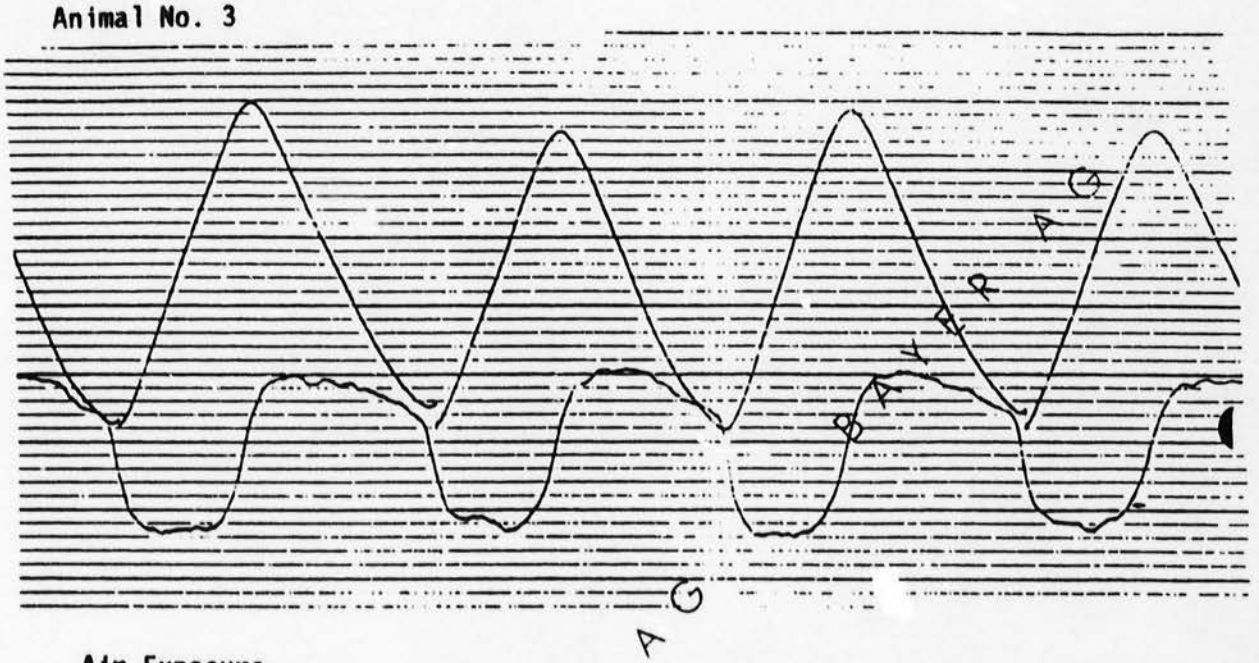
DESMODUR VP PU 1806

Study-no.: T6039897

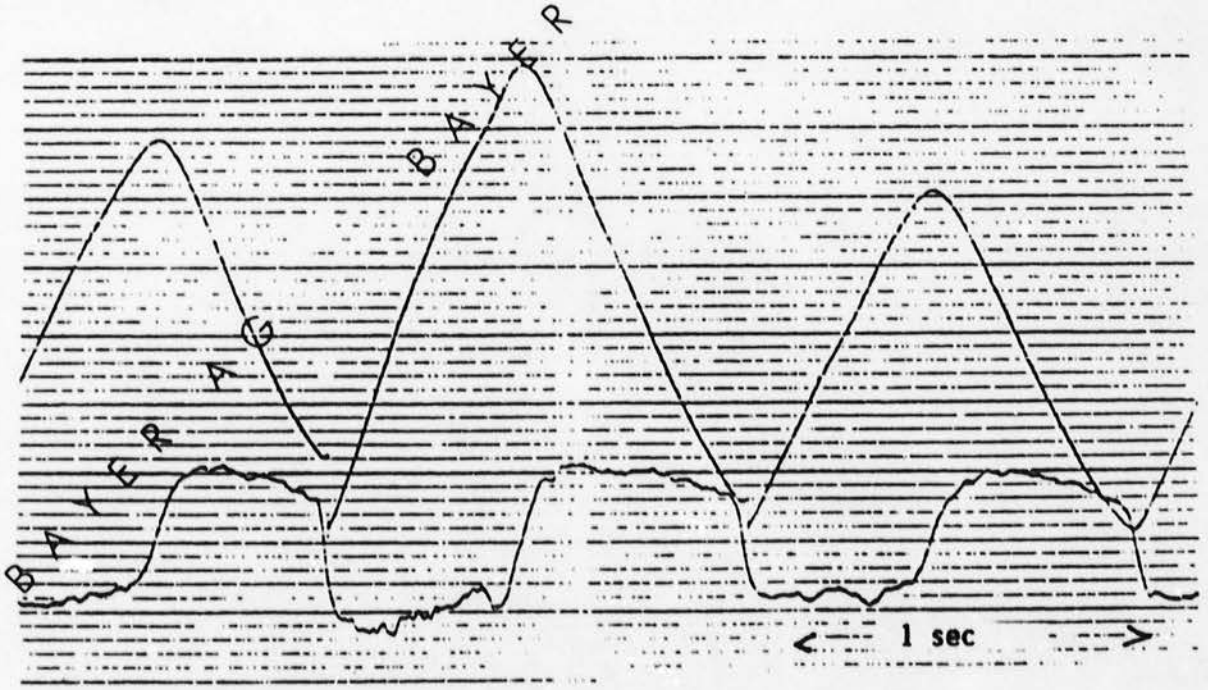


Respiration Cycle - DESMODUR VP PU 1806 Challenge
- Control

Animal No. 3



Air Exposure

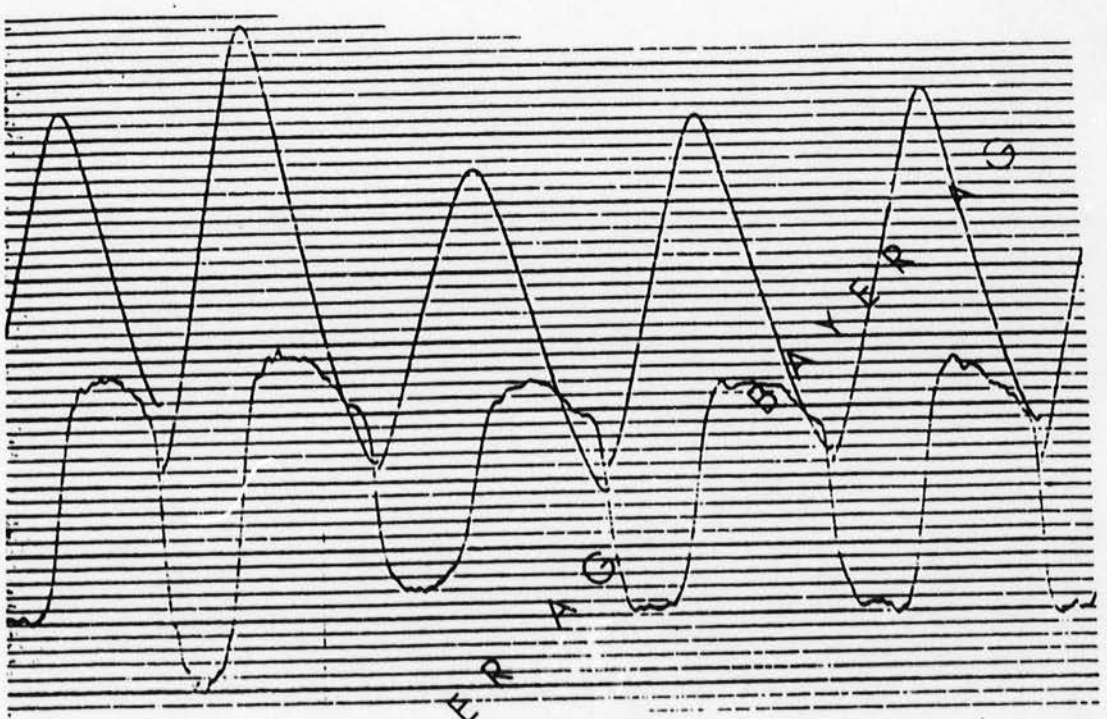


After 23-min exposure to MDI

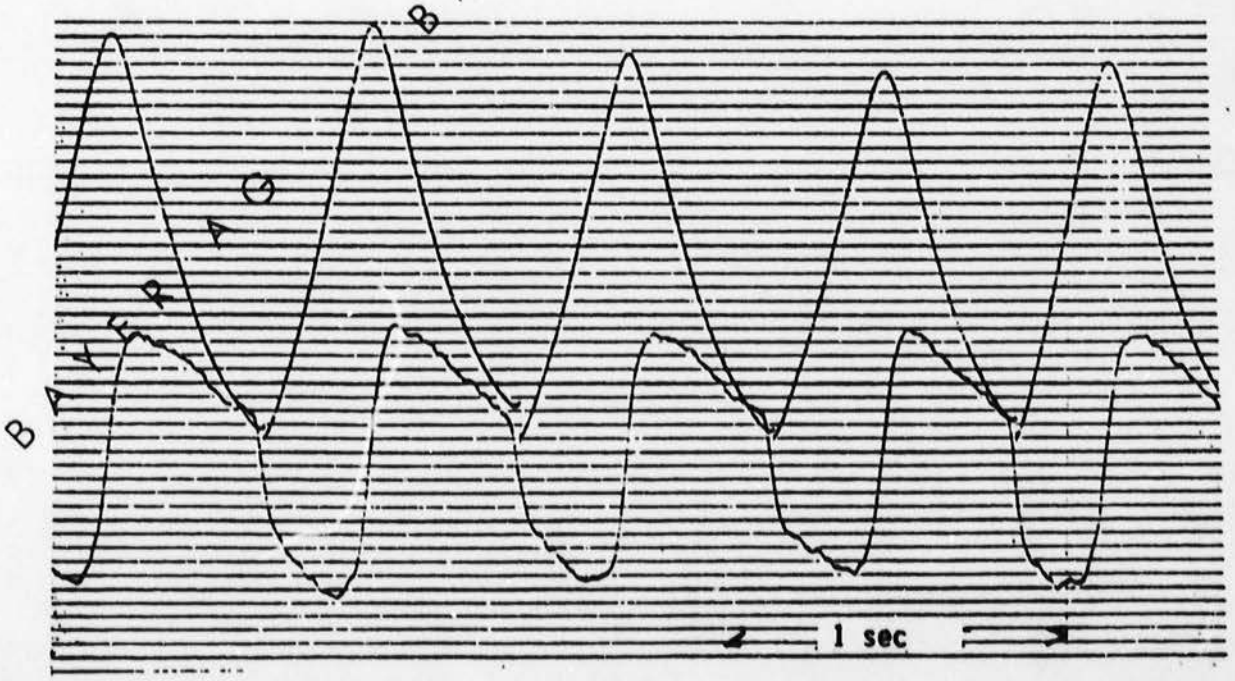
For key, see p. 26

DESMODUR VP PU 1806 Group

Animal No. 15

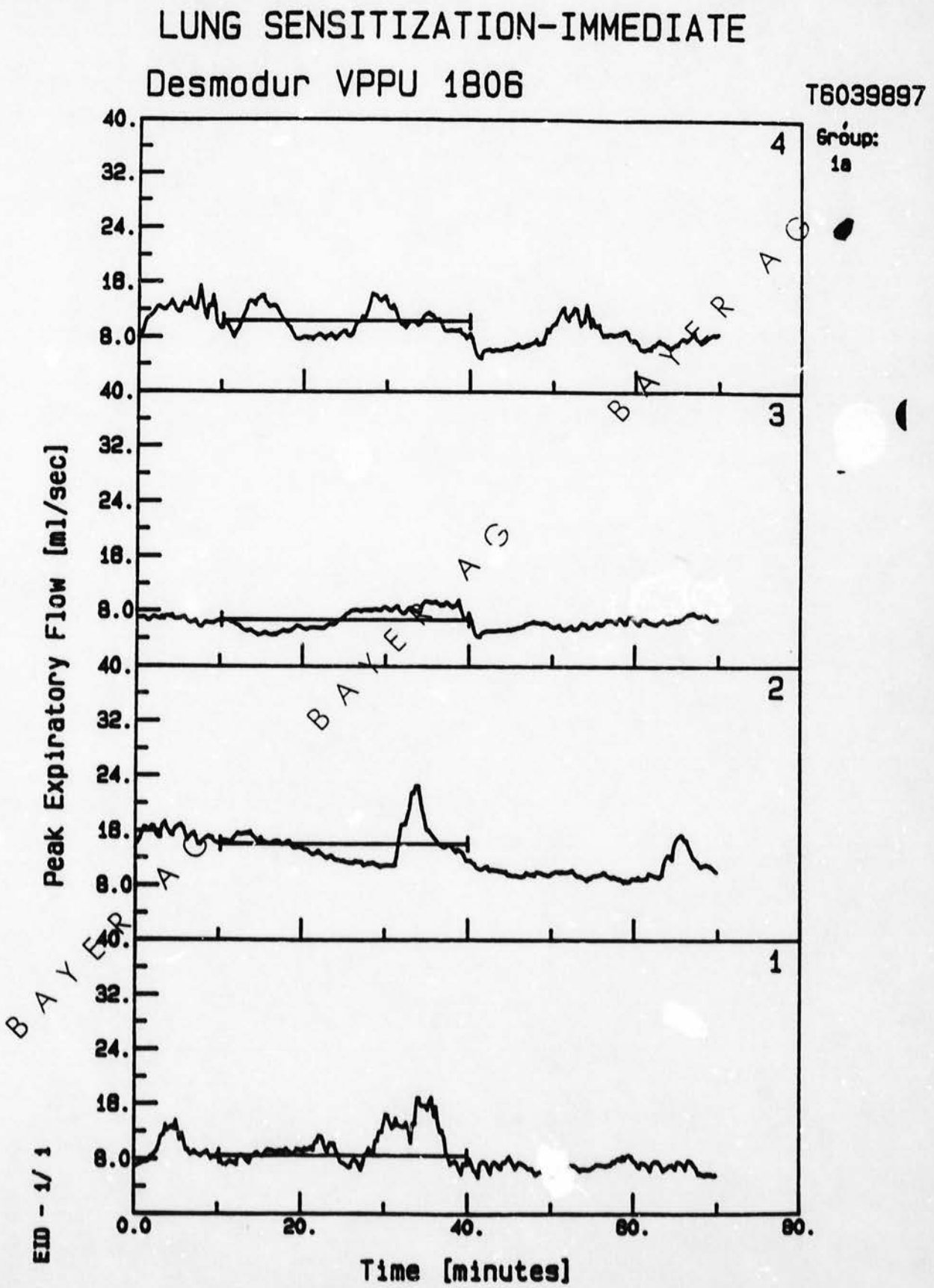


Air Exposure



After 21-min exposure to MDI

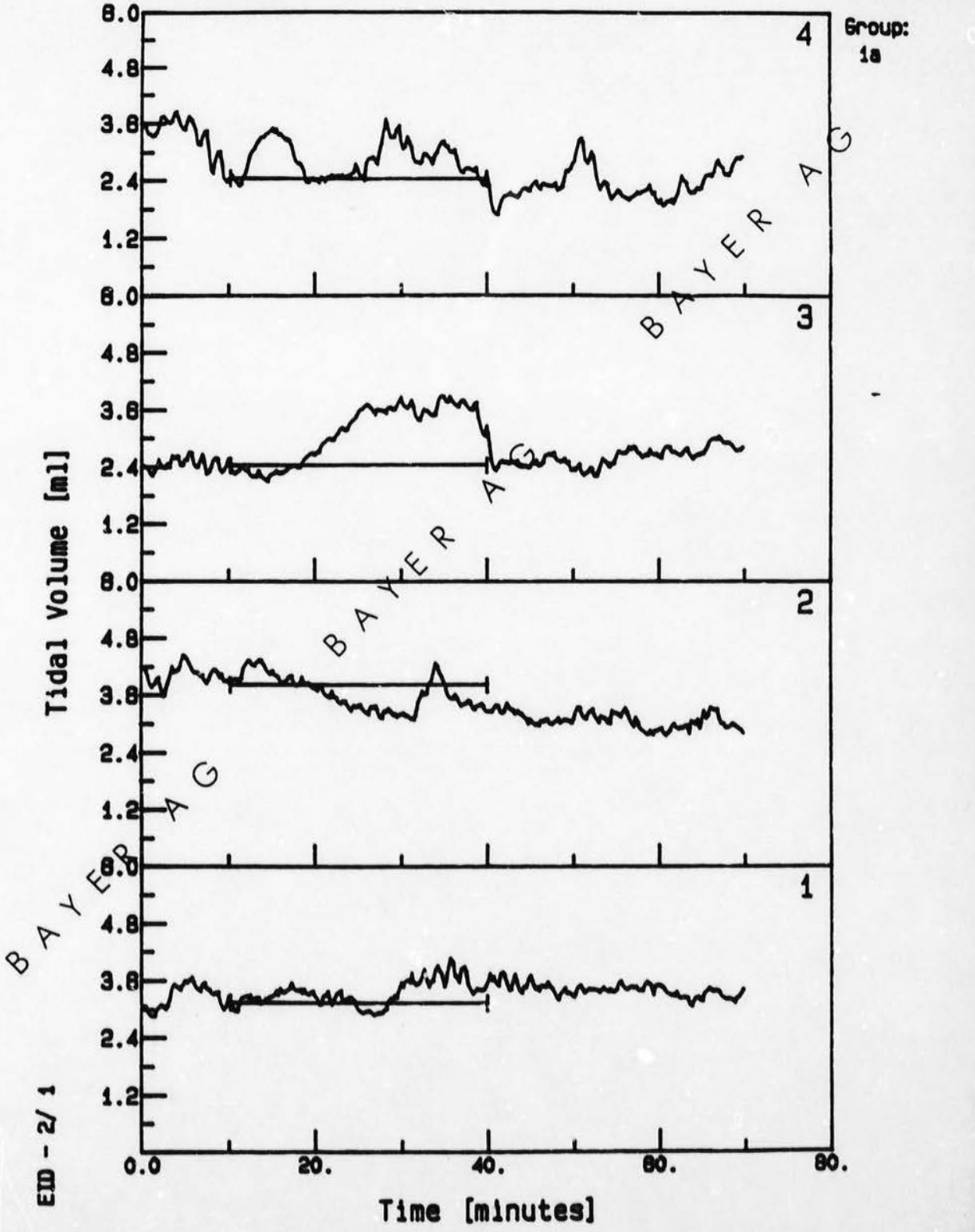
For key, see p. 26


LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
1a
4
3
2
1
40.
32.
24.
18.
8.0
Peak Expiratory Flow [ml/sec]
EM - 1/ 1
0.0
20.
40.
60.
80.
Time [minutes]
BAYER AG

LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

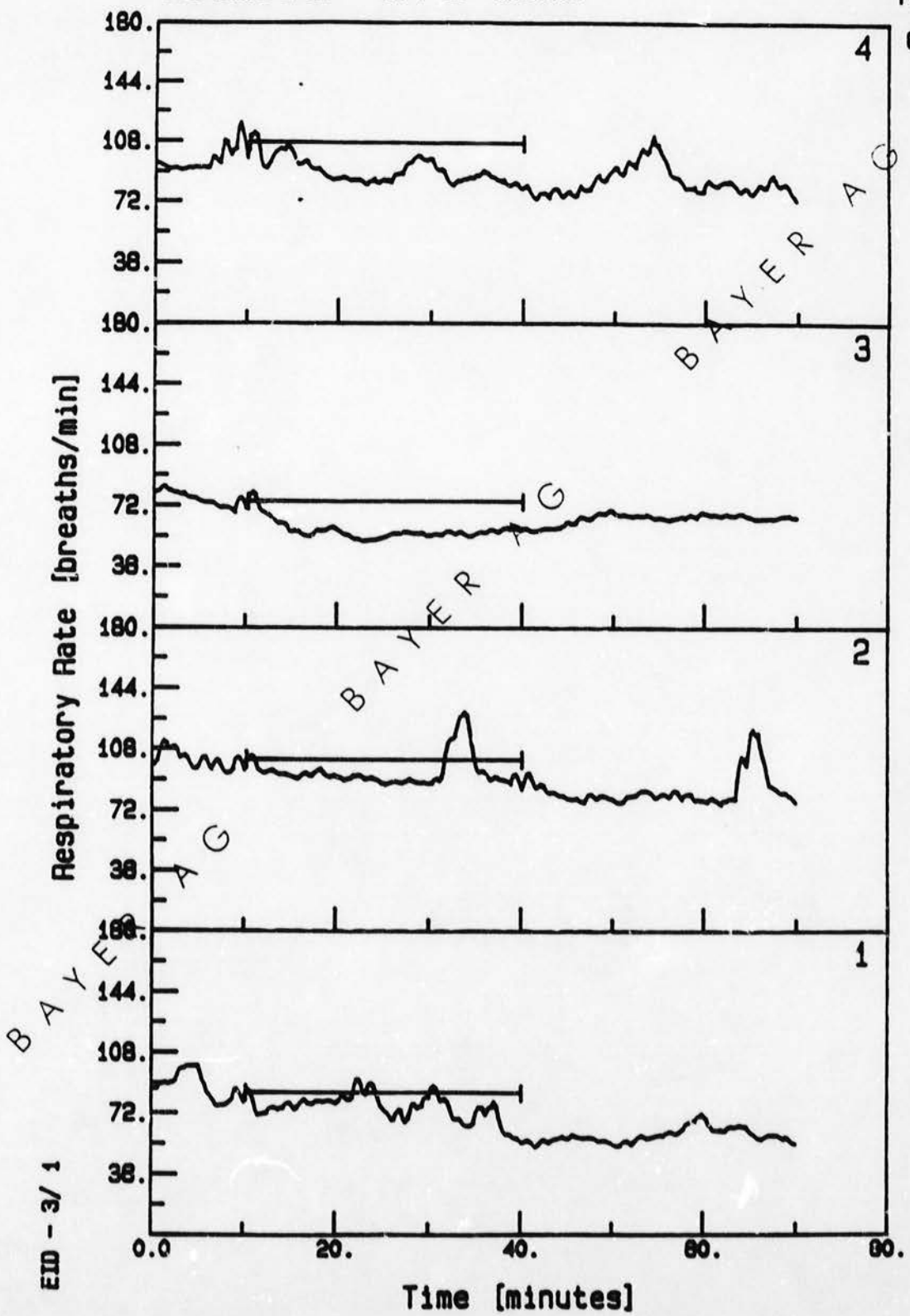
T6039897



LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

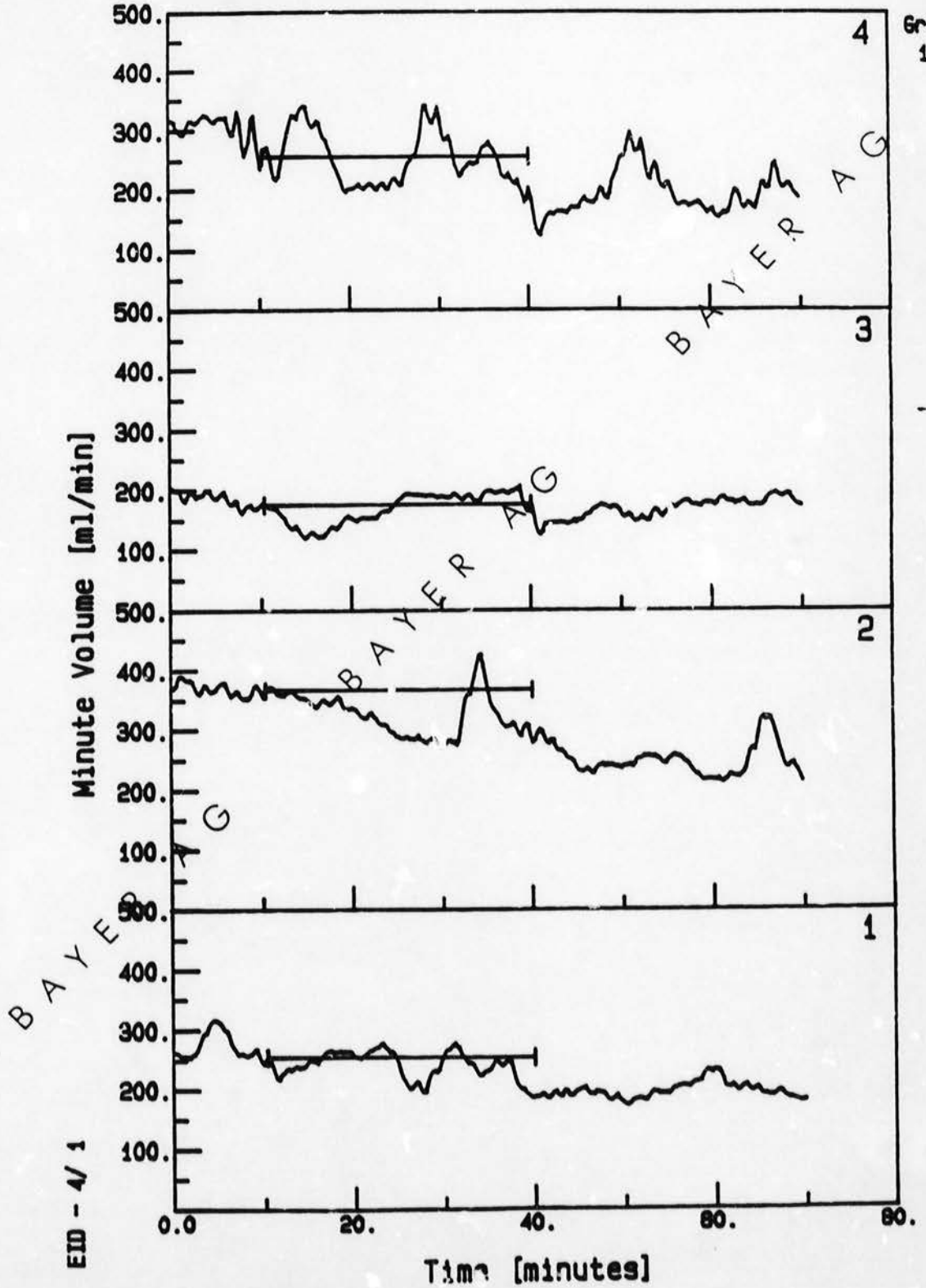
T6039897



LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

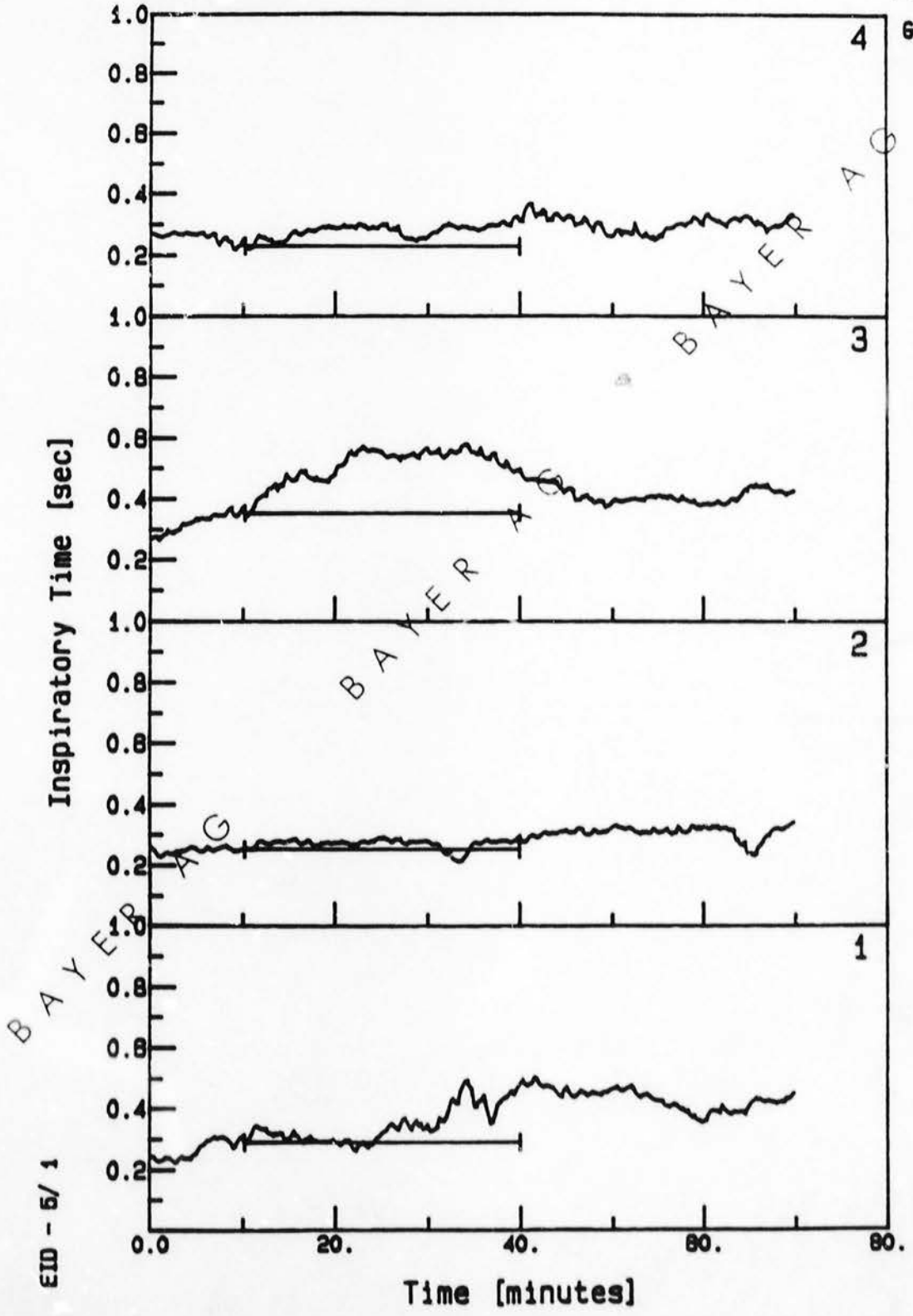
T6039897



LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

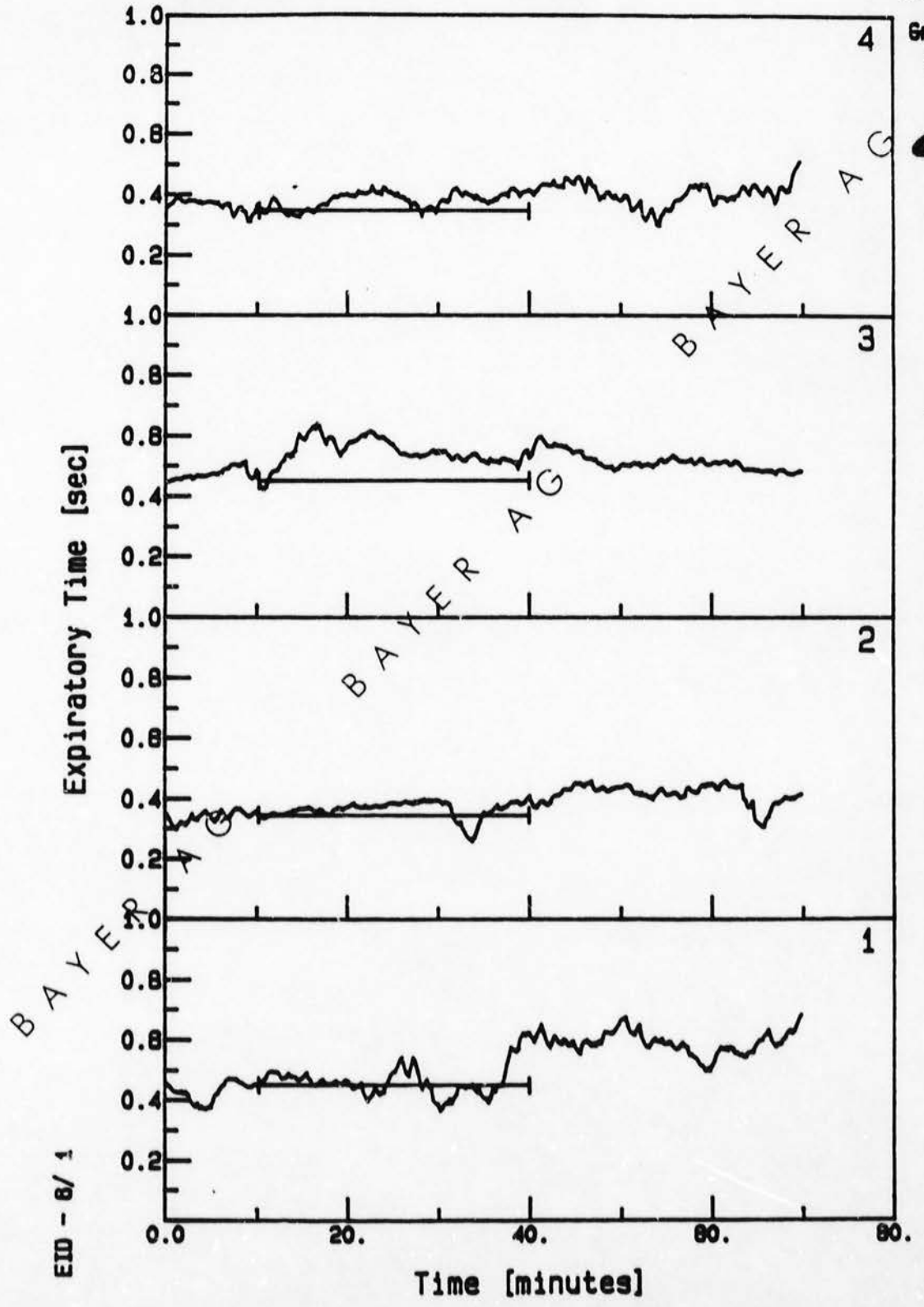
T6039897



LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

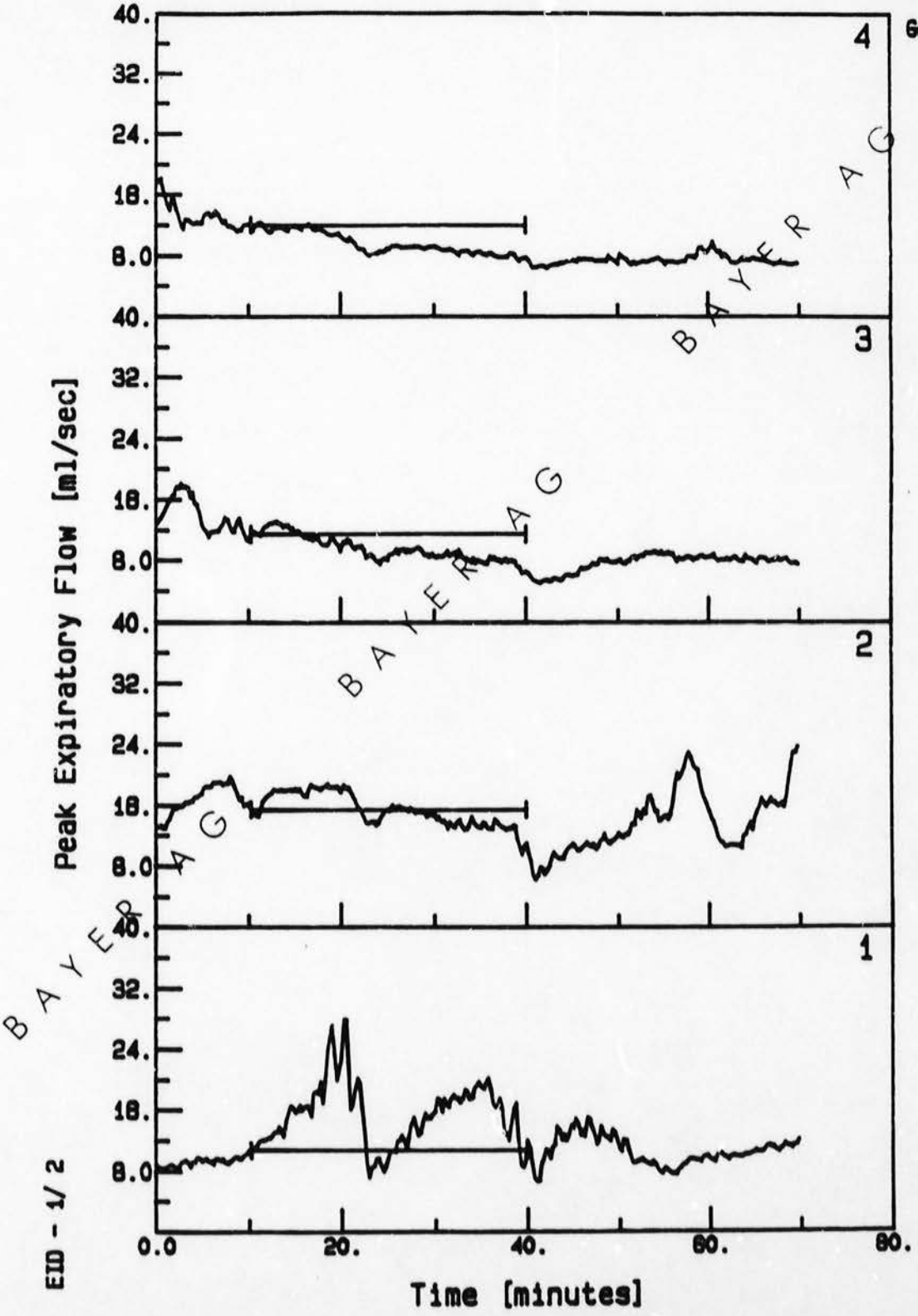
T6039897



LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

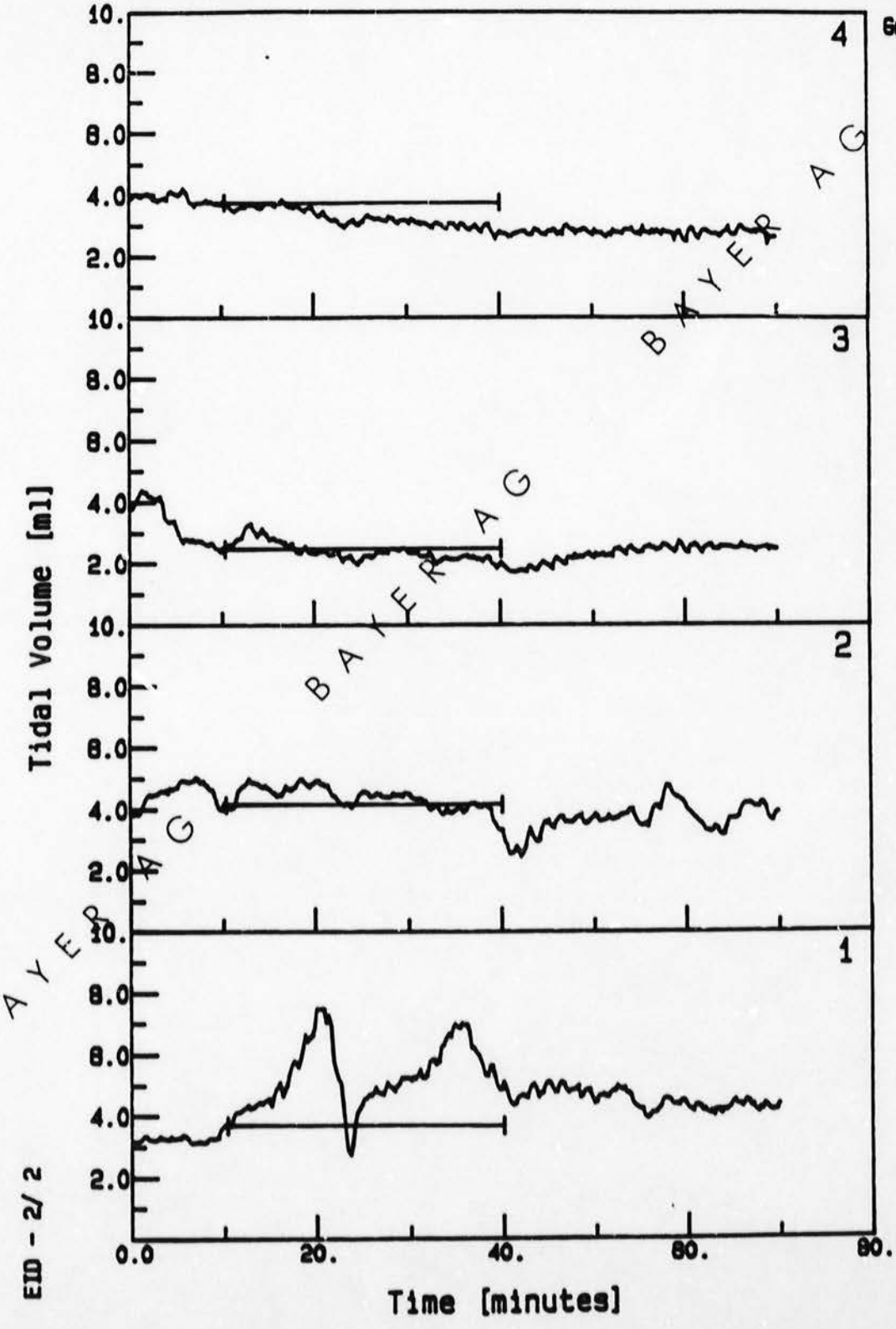
T6039897

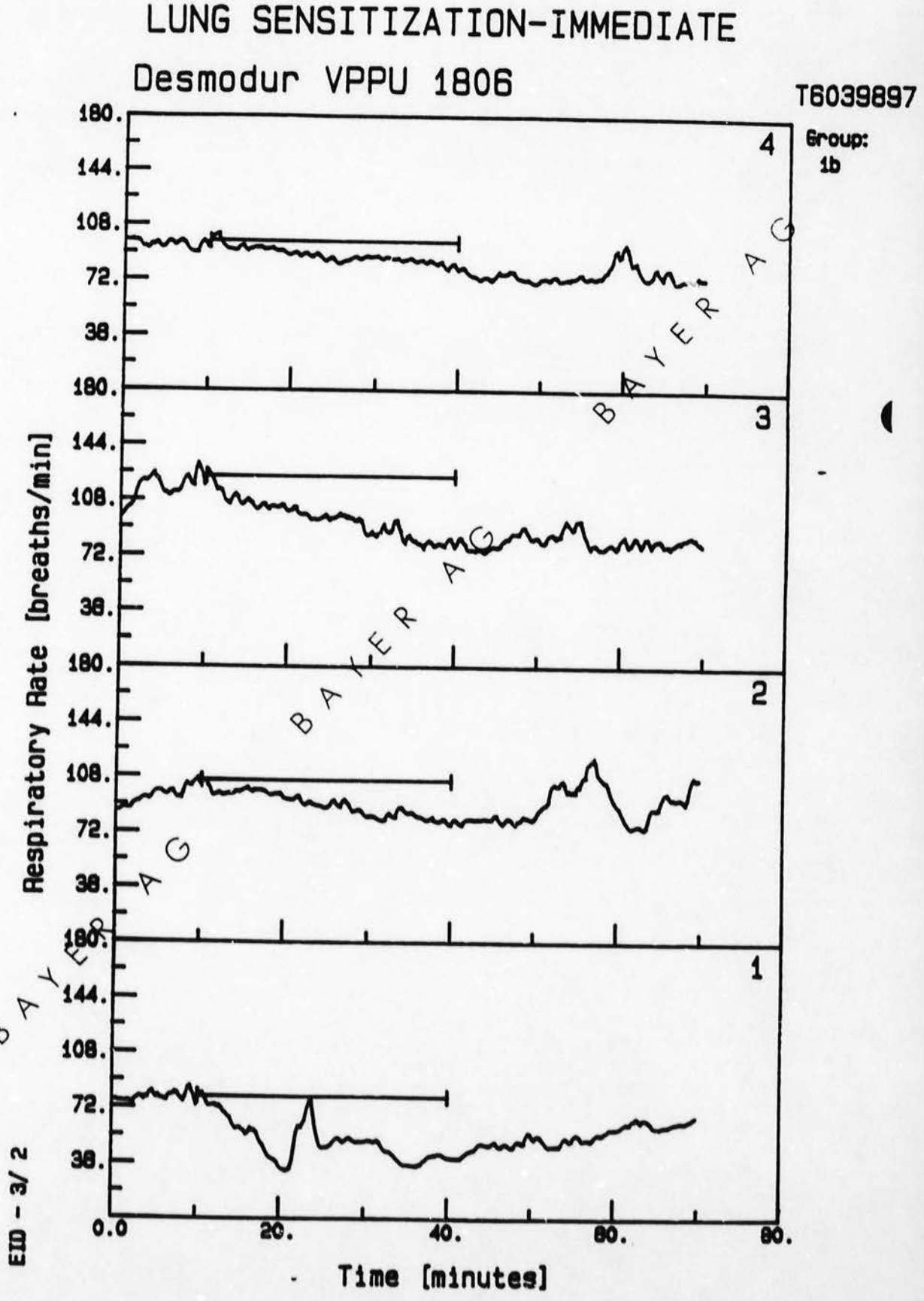


LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

T6039897

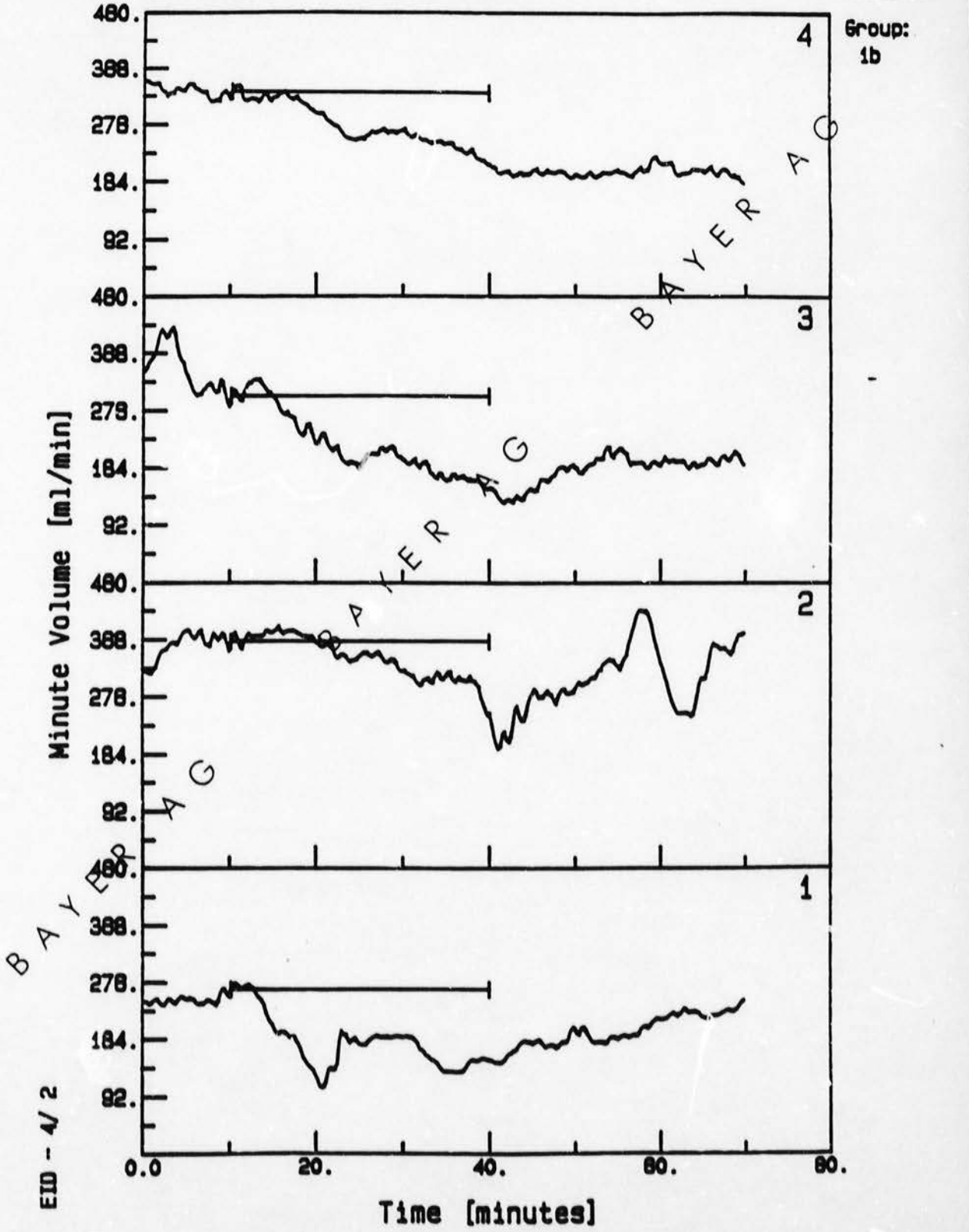



LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
1b
4
3
2
1
180.
144.
108.
72.
36.
Respiratory Rate [breaths/min]
0.0
20.
40.
60.
80.
Time [minutes]
EID - 3/ 2
BAYER AG

LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

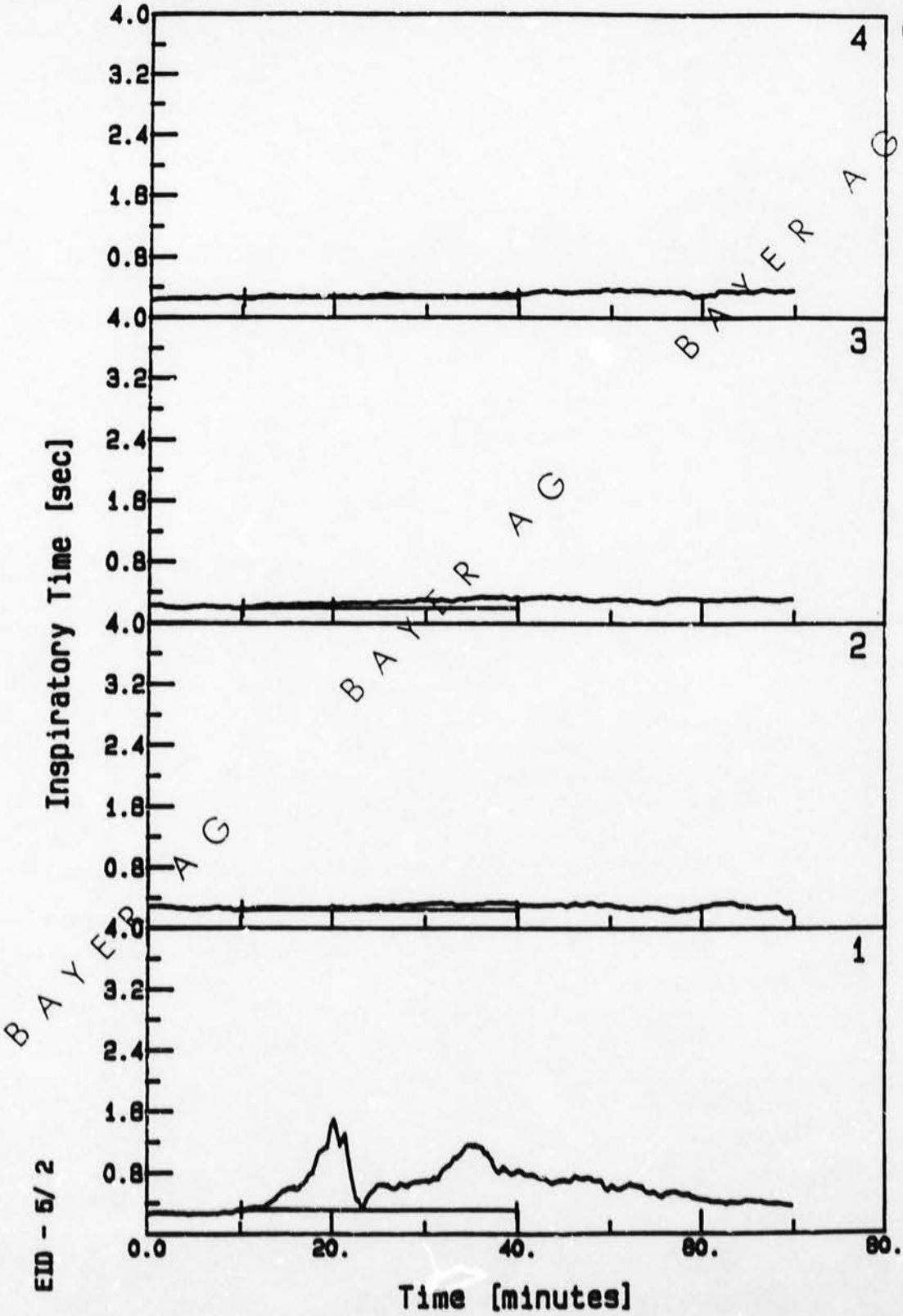
T6039897



LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

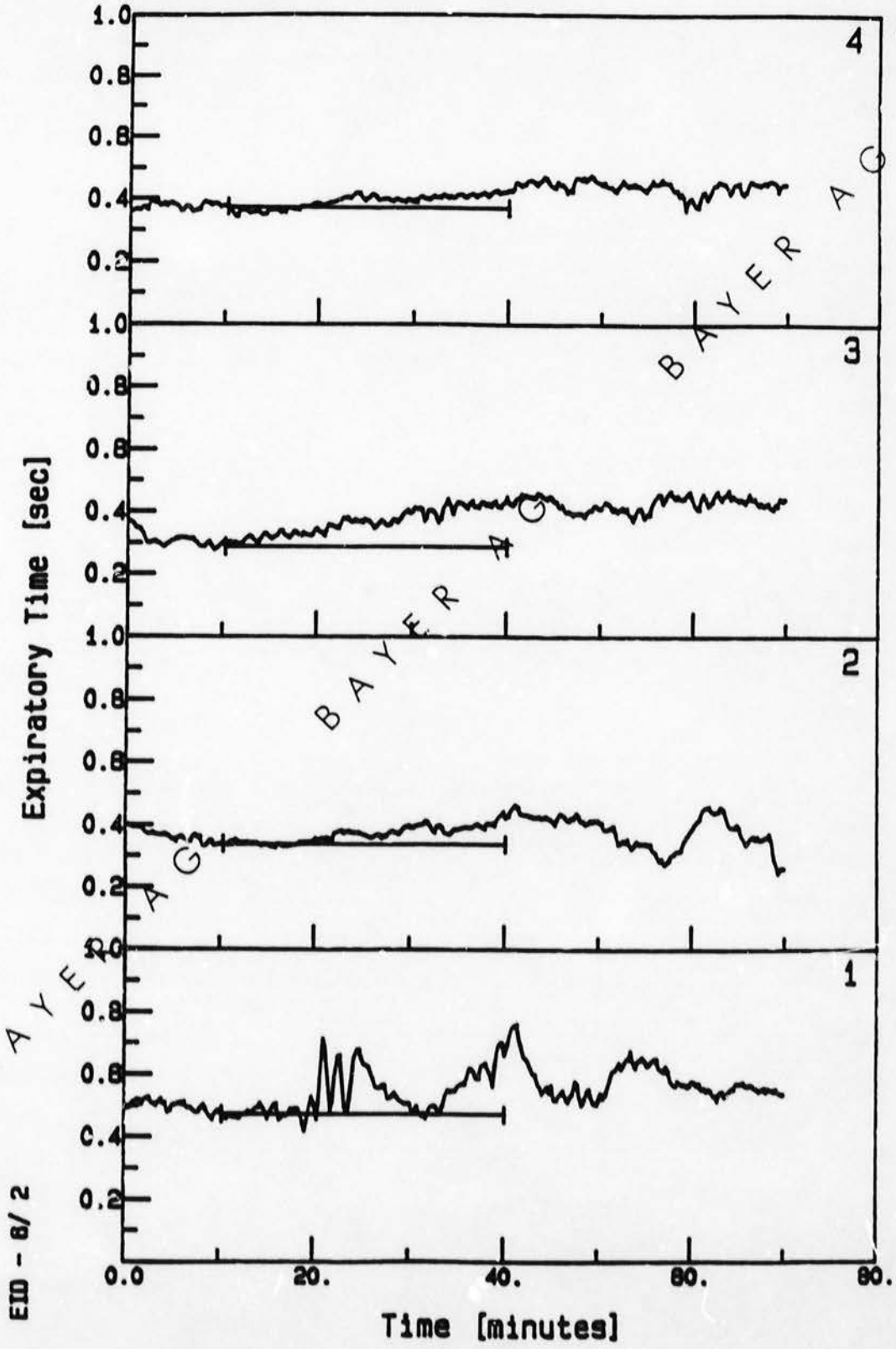
T6039897

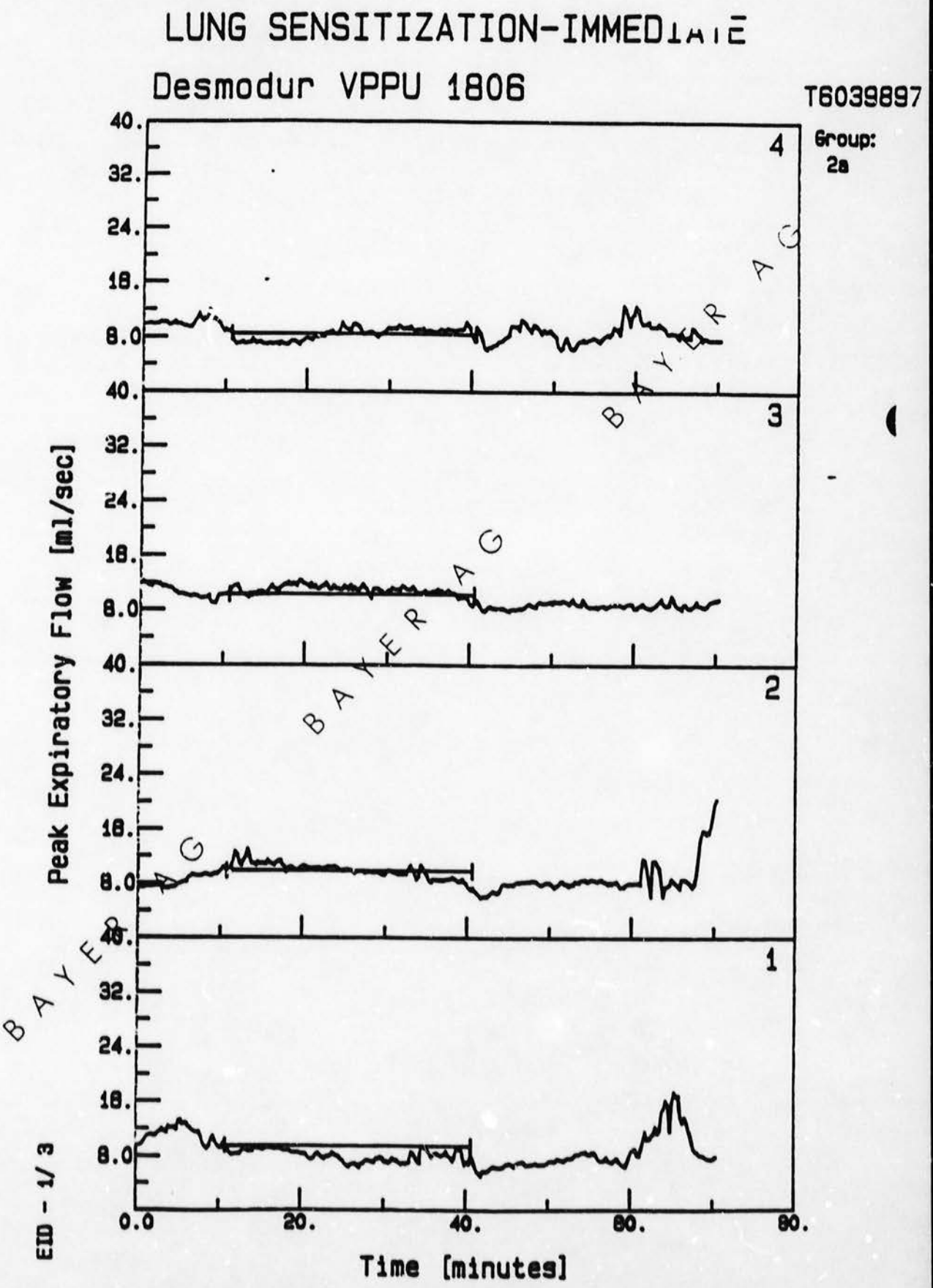


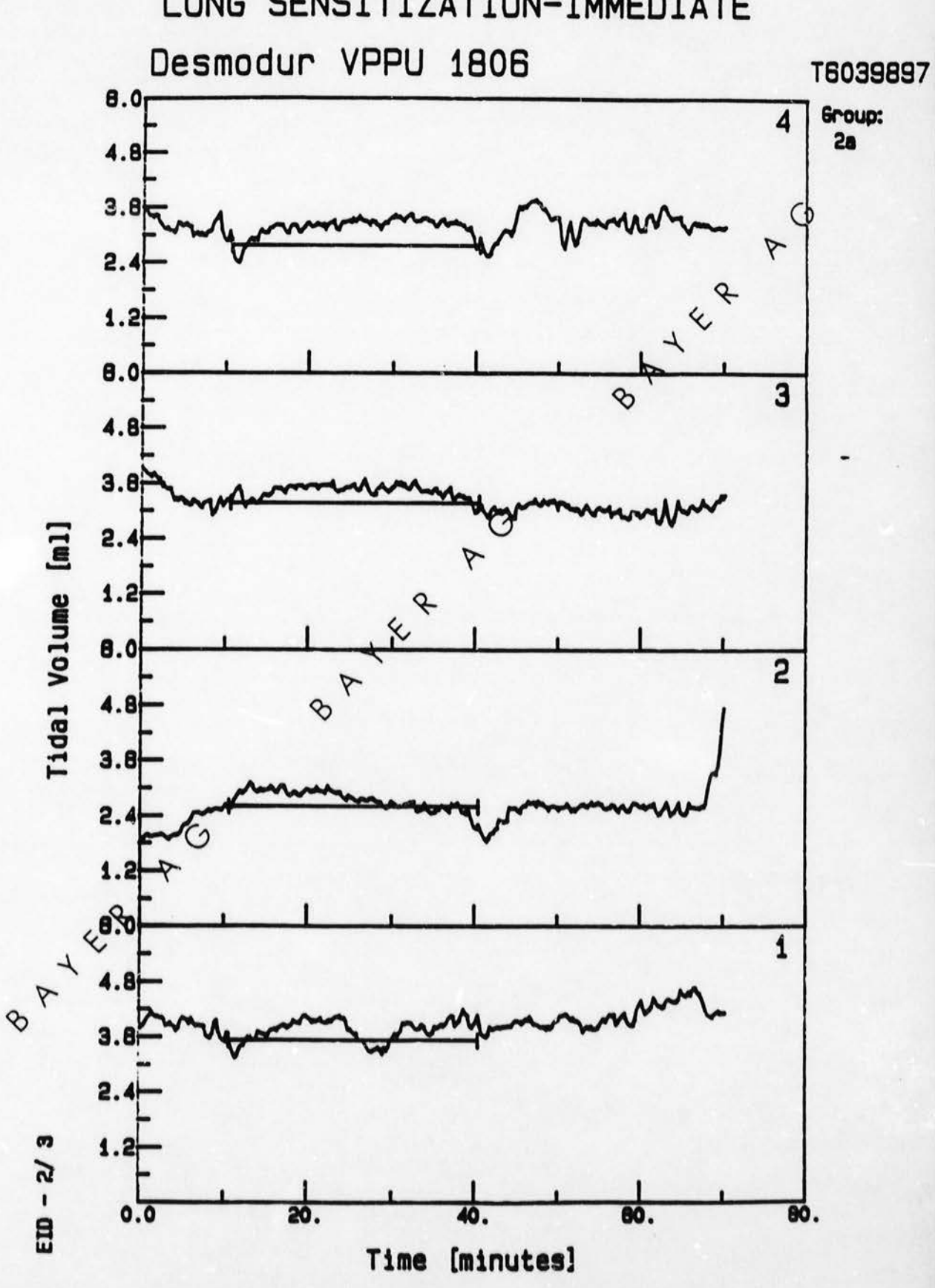
LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

T6039897



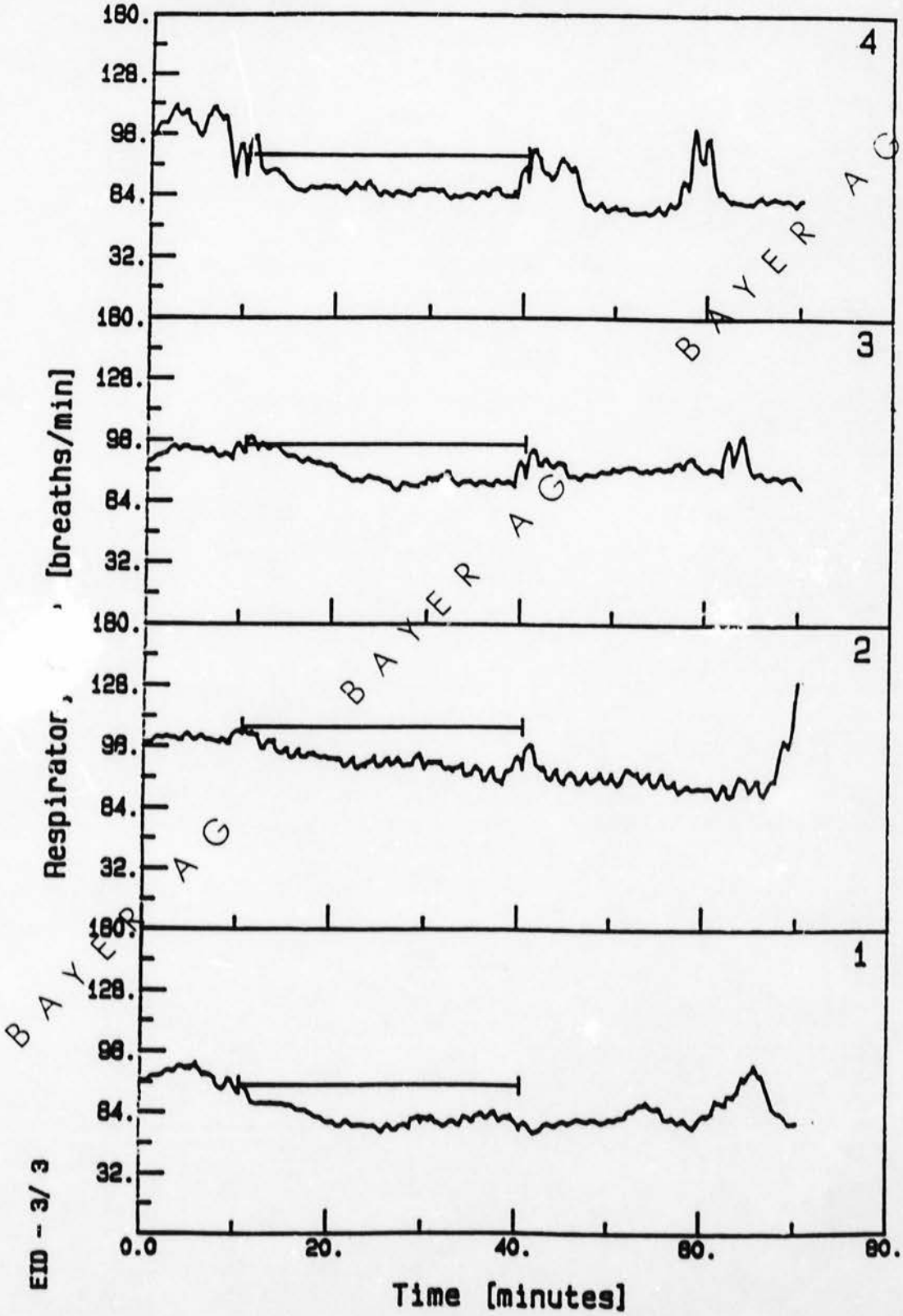

LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
2a
4
3
2
1
Peak Expiratory Flow [ml/sec]
EID - 1/3
Time [minutes]
0.0
20.
40.
60.
80.
8.0
18.
24.
32.
40.
BAYER AG

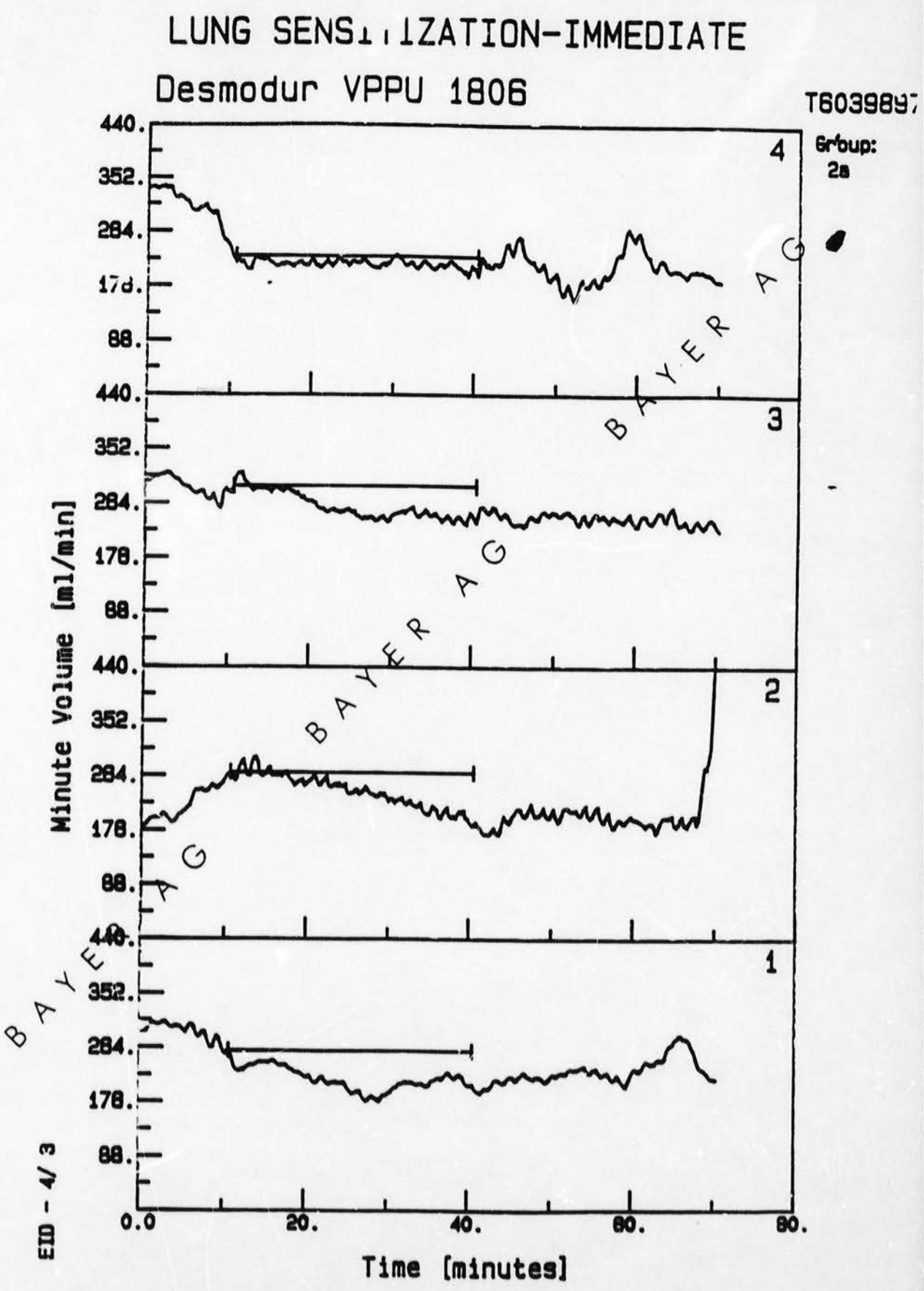

LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
2a
4
3
2
1
8.0
4.8
3.8
2.4
1.2
0.0
Tidal Volume [ml]
BAYER AG
EM - 2/ 3
0.0
20.
40.
60.
80.
Time [minutes]

LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

T6039897

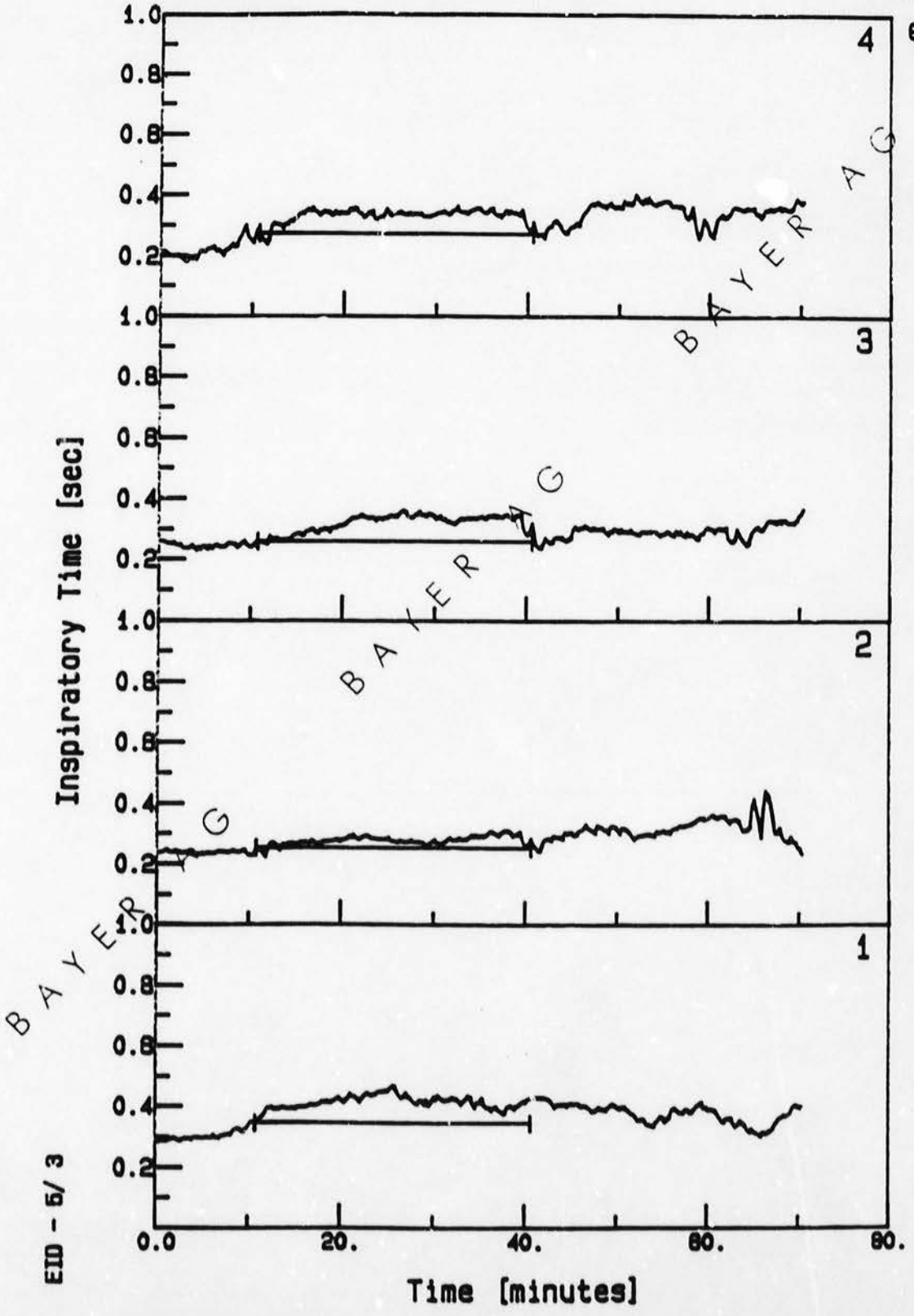



LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
2a
4
3
2
1
440.
352.
284.
176.
88.
Minute Volume [ml/min]
0.0
20.
40.
60.
80.
Time [minutes]
EID - 4/ 3
BAYER AG

LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

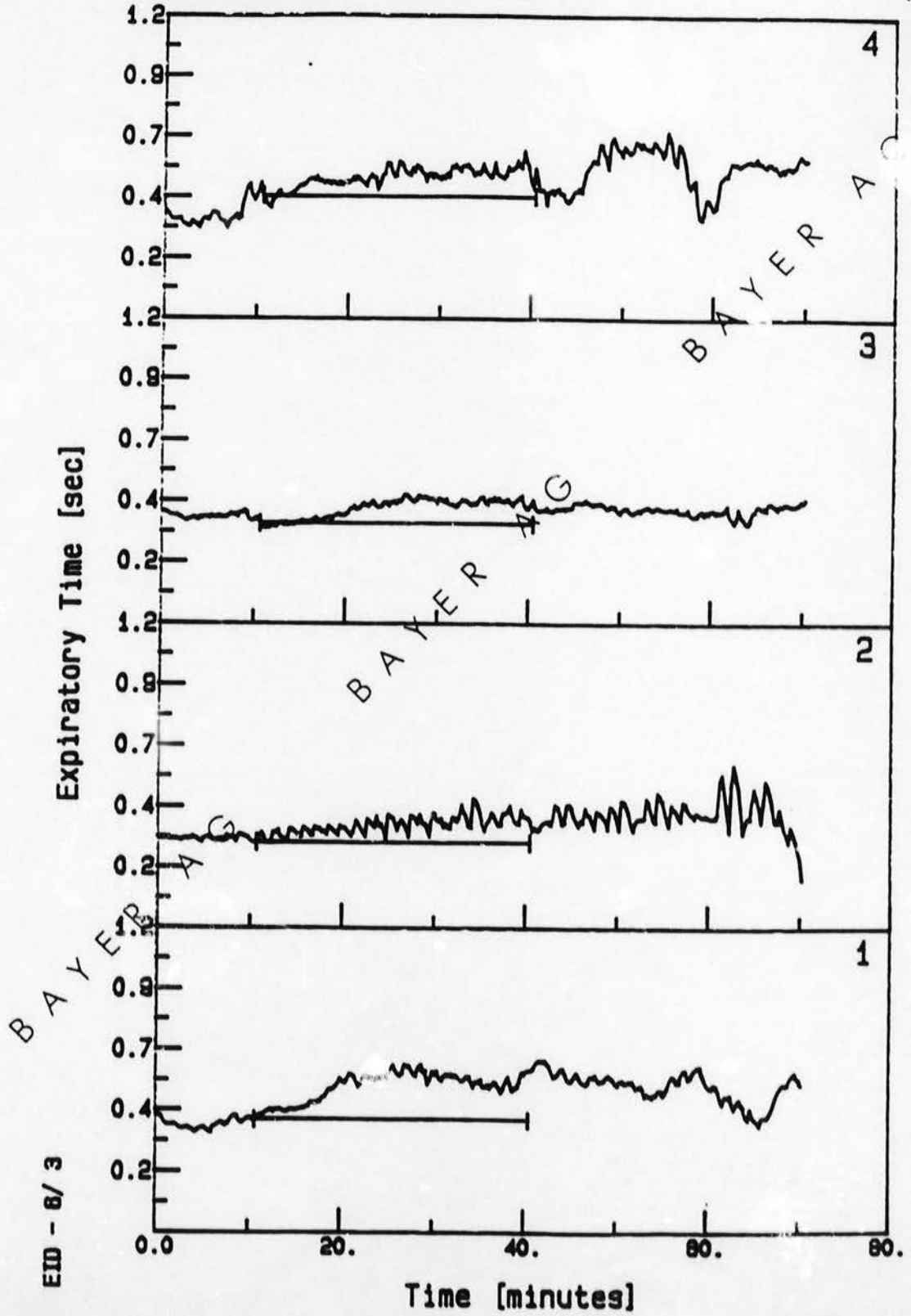
T6039897

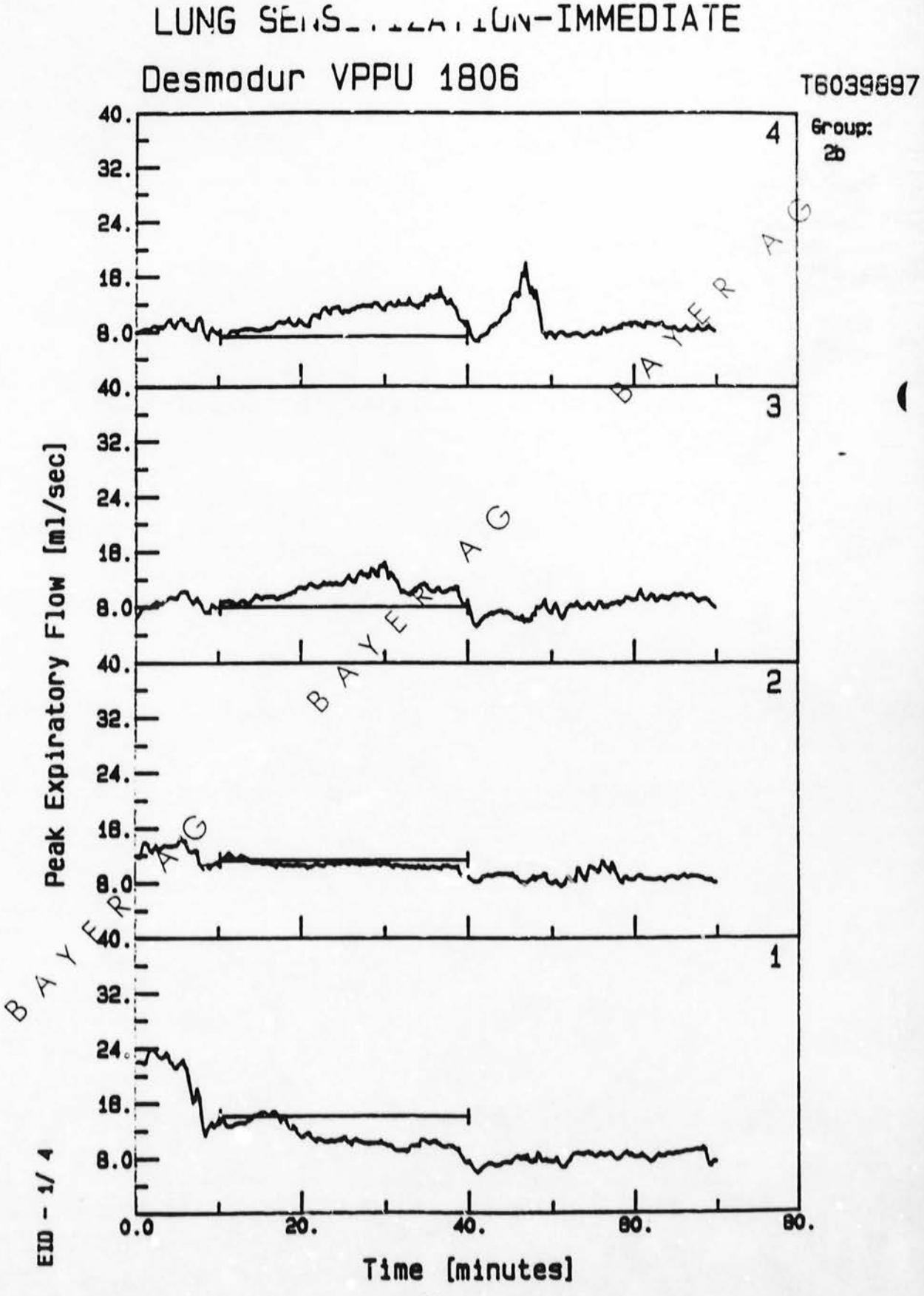


LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

T6039897

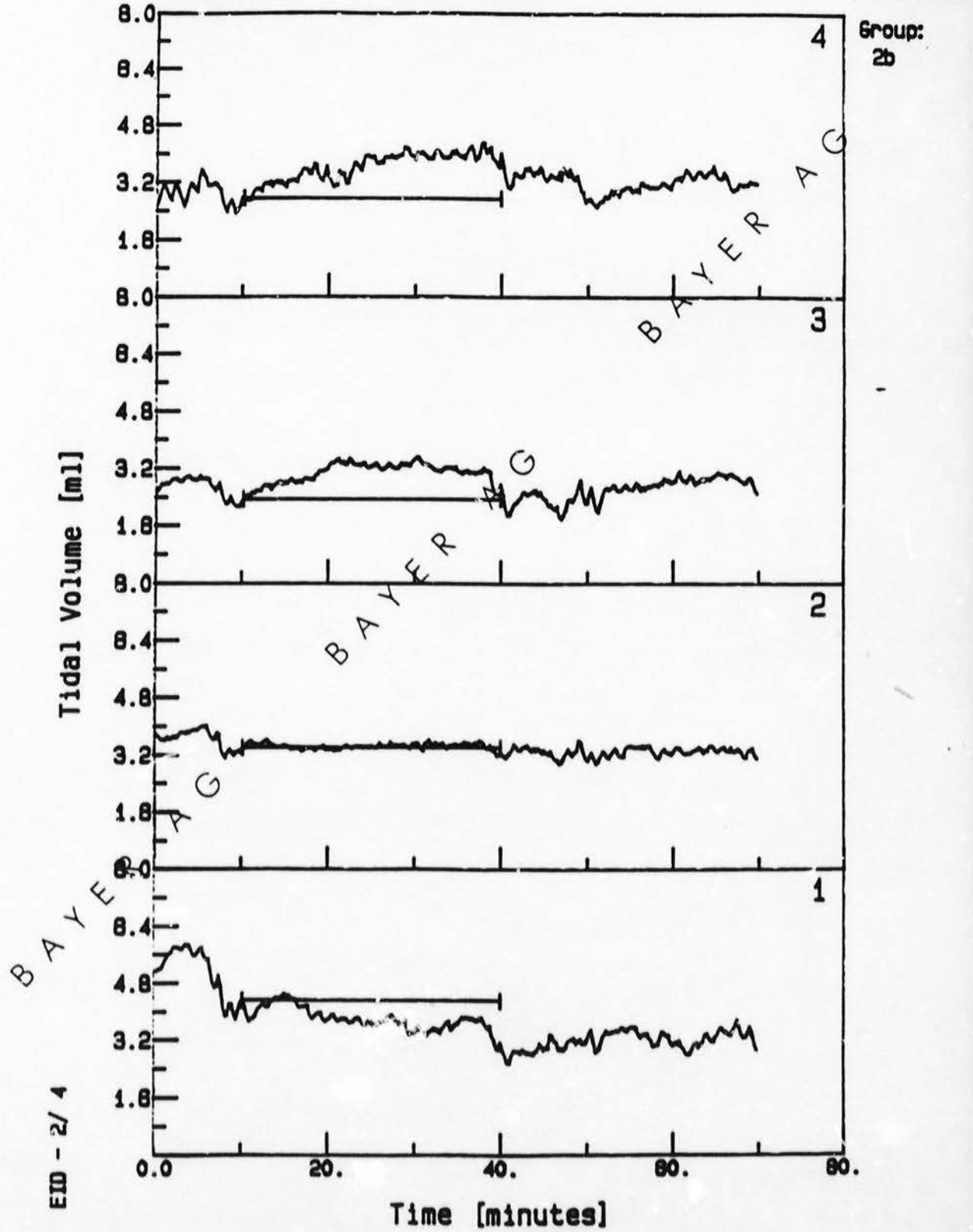


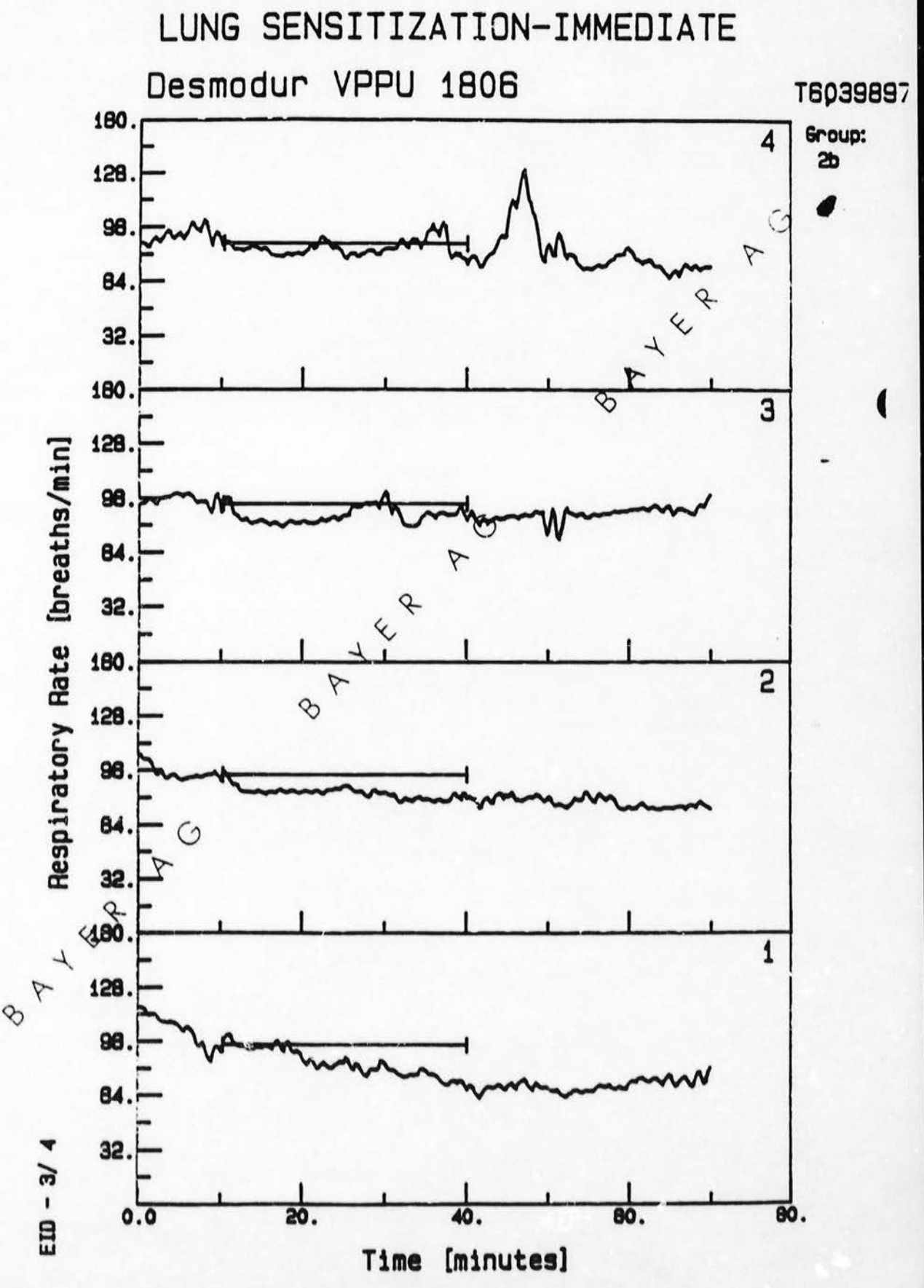

LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
2b
4
3
2
1
40.
32.
24.
18.
8.0
Peak Expiratory Flow [ml/sec]
0.0
20.
40.
60.
80.
Time [minutes]
EID - 1/ 4
BAYER AG

LUNG SENSITIZATION-IN :DIATE

Desmodur VPPU 1806

T6039897



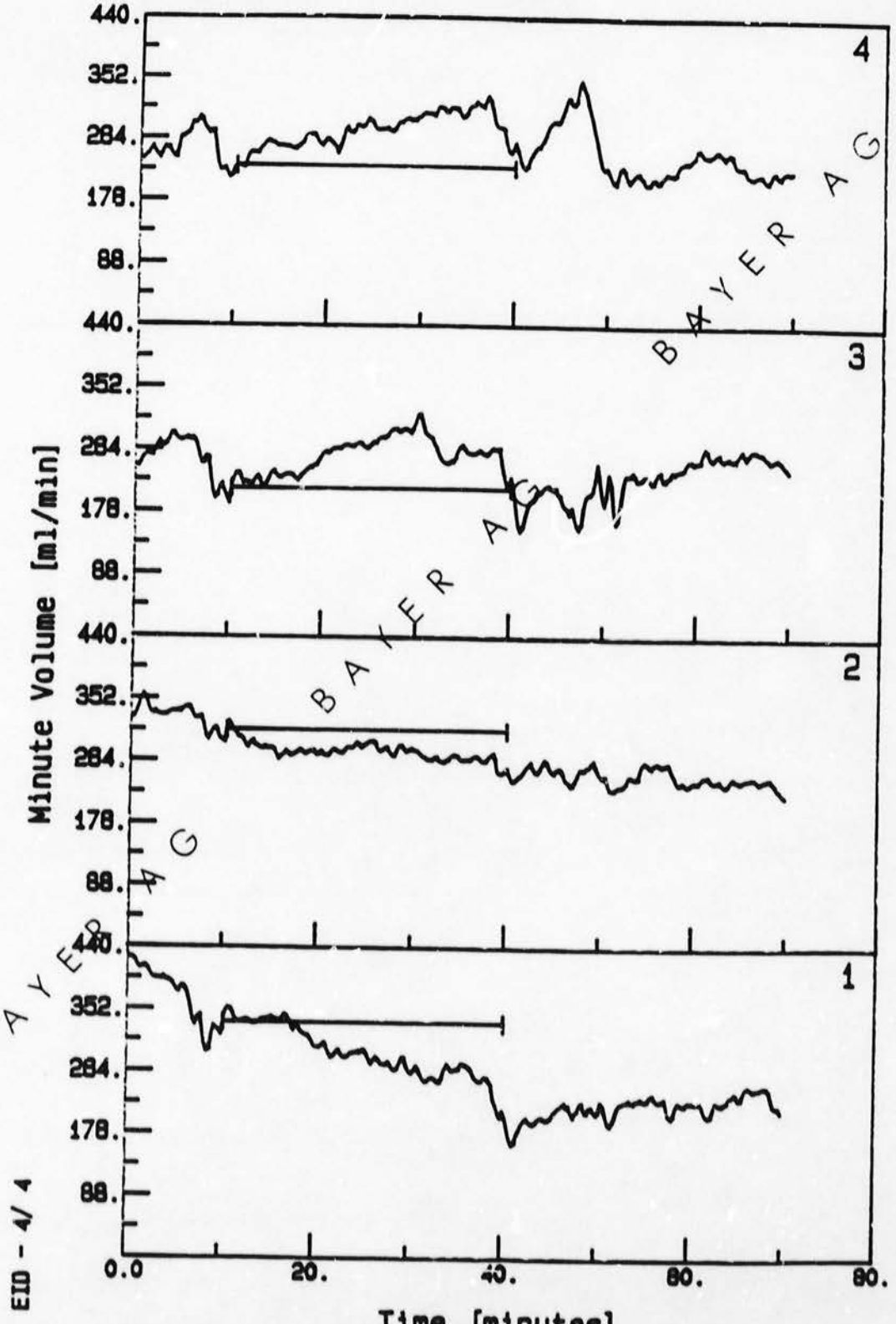

LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
2b
4
3
2
1
180.
128.
96.
64.
32.
Respiratory Rate [breaths/min]
0.0
20.
40.
60.
80.
Time [minutes]
EID - 3/ 4
BAYER AG

LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

T603989

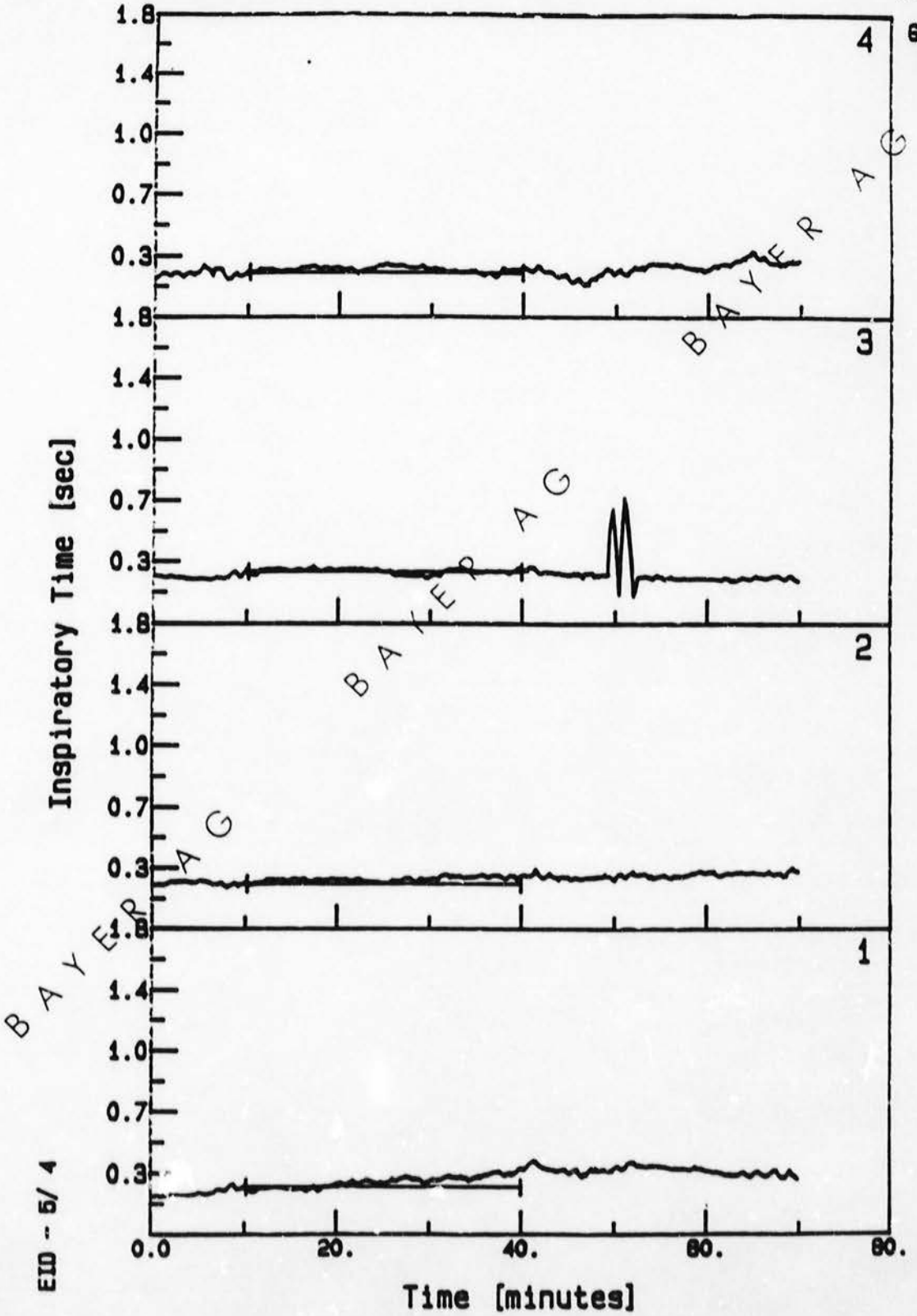
Group: 2b

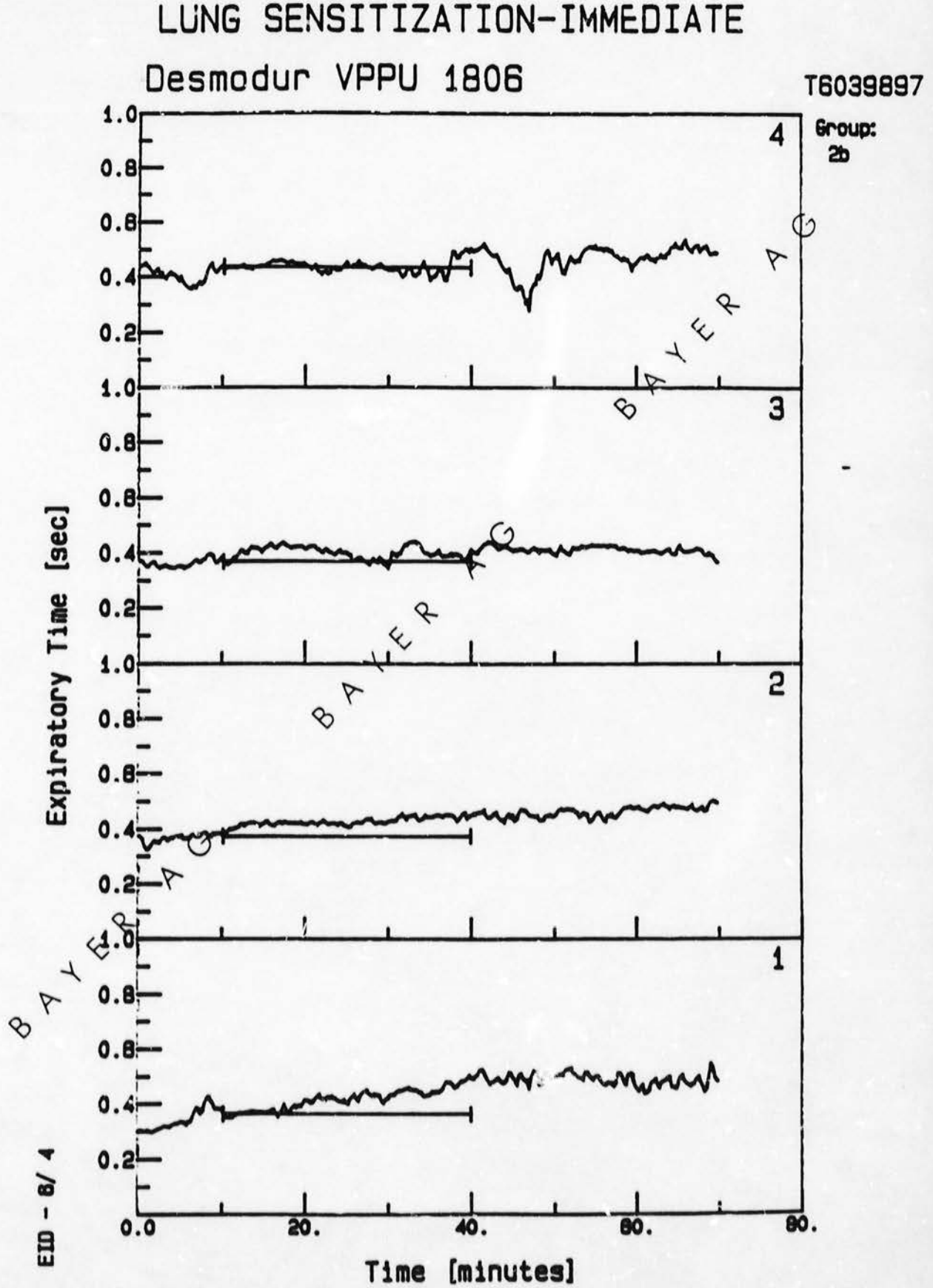


LUNG SENSITIZATION-IMMEDIATE

Desmodur VPPU 1806

T6039897




LUNG SENSITIZATION-IMMEDIATE
Desmodur VPPU 1806
T6039897
Group:
2b
4
3
2
1
Expiratory Time [sec]
1.0
0.8
0.6
0.4
0.2
0.0
20.
40.
60.
80.
Time [minutes]
EID - 6/ 4
BAYER AG

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

SUMMARY TABLE

(Data relative to control-period in %)

Group:	Min./ Max.	PEF	TV	RATE	MV	IT	ET
1a	min.	57.0	82.4	74.8	64.1	89.9	96.6
	max.	130.6	112.9	106.8	106.0	148.4	129.0
1b	min.	46.2	74.7	70.8	52.9	95.2	93.3
	max.	126.8	120.7	109.5	105.4	129.5	136.3
2a	min.	62.5	85.6	73.5	74.1	93.0	94.3
	max.	119.2	116.4	105.0	105.0	141.8	140.5
2b	min.	52.3	71.8	75.3	64.6	94.5	95.0
	max.	114.2	112.1	104.8	107.1	161.2	131.4

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
1	00:00:15	.3	9.05	3.32	90.8	294.3	.25	.39
2	00:00:30	.5	9.85	3.26	92.6	295.7	.25	.39
3	00:00:45	.8	10.25	3.01	96.2	288.4	.24	.39
4	00:01:00	1.0	10.65	3.14	93.7	283.2	.25	.39
5	00:01:15	1.3	10.03	3.07	93.1	277.1	.26	.40
6	00:01:30	1.5	10.05	3.18	91.5	277.6	.26	.40
7	00:01:45	1.8	10.48	3.17	91.9	281.8	.26	.40
8	00:02:00	2.0	10.50	3.16	93.3	284.5	.26	.40
9	00:02:15	2.3	10.55	2.94	94.1	278.9	.24	.39
10	00:02:30	2.5	9.80	3.03	93.7	271.5	.25	.40
11	00:02:45	2.8	10.83	3.24	92.7	281.7	.26	.39
12	00:03:00	3.0	11.60	3.44	92.1	295.3	.26	.39
13	00:03:15	3.3	12.80	3.34	94.5	298.8	.26	.39
14	00:03:30	3.5	11.48	3.51	91.8	297.0	.28	.40
15	00:03:45	3.8	10.95	3.30	90.7	292.5	.26	.40
16	00:04:00	4.0	11.63	3.37	91.4	290.5	.27	.39
17	00:04:15	4.3	12.28	3.31	92.9	297.6	.26	.39
18	00:04:30	4.5	11.83	3.35	93.2	291.2	.27	.39
19	00:04:45	4.8	12.60	3.76	93.5	300.7	.28	.39
20	00:05:00	5.0	13.63	3.55	94.4	309.3	.27	.37
21	00:05:15	5.3	12.13	3.65	92.2	309.2	.28	.39
22	00:05:30	5.5	12.06	3.67	90.0	305.9	.28	.39
23	00:05:45	5.8	12.15	3.46	89.6	301.2	.28	.40
24	00:06:00	6.0	11.05	3.48	87.5	290.3	.29	.41
25	00:06:15	6.3	11.05	3.49	86.6	288.3	.29	.41
26	00:06:30	6.5	11.53	3.38	87.7	286.5	.28	.41
27	00:06:45	6.8	11.23	3.46	88.1	286.1	.30	.41
28	00:07:00	7.0	11.17	3.49	85.6	285.2	.30	.42
29	00:07:15	7.3	10.60	3.16	88.0	278.8	.28	.41
30	00:07:30	7.5	10.98	3.03	91.1	269.9	.28	.42
31	00:07:45	7.8	9.20	3.11	84.3	252.3	.30	.44
32	00:08:00	8.0	10.28	3.21	84.0	257.1	.30	.42
33	00:08:15	8.3	11.10	3.41	86.5	273.4	.29	.42
34	00:08:30	8.5	11.88	3.29	90.3	279.5	.28	.42
35	00:08:45	8.8	10.13	3.20	87.3	276.3	.30	.42
36	00:09:00	9.0	10.20	3.18	85.6	267.7	.29	.42
37	00:09:15	9.3	10.10	3.16	85.4	263.6	.30	.42
38	00:09:30	9.5	10.25	3.03	84.8	254.3	.29	.42
39	00:09:45	9.8	10.68	3.22	86.7	266.1	.29	.41
40	00:10:00	10.0	10.95	3.24	87.5	279.1	.28	.41
1	00:00:15	10.3	10.98	2.55	120.0	308.4	.21	.32
2	00:00:30	10.5	9.68	2.78	105.8	280.9	.25	.37

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
3	00:00:45	10.8	9.00	2.74	97.9	262.8	.28	.39
4	00:01:00	11.0	8.95	2.84	90.8	247.3	.30	.41
5	00:01:15	11.3	8.50	2.83	85.9	237.2	.31	.42
6	00:01:30	11.5	8.88	2.99	83.6	239.3	.31	.43
7	00:01:45	11.8	9.10	3.13	80.2	232.6	.33	.45
8	00:02:00	12.0	9.18	3.01	80.6	234.7	.32	.42
9	00:02:15	12.3	9.65	3.16	81.2	245.0	.32	.43
10	00:02:30	12.5	10.30	3.23	81.0	248.4	.32	.43
11	00:02:45	12.8	9.83	3.08	82.6	250.0	.32	.42
12	00:03:00	13.0	10.03	3.22	82.1	254.5	.33	.43
13	00:03:15	13.3	10.52	3.27	83.4	260.5	.31	.42
14	00:03:30	13.5	10.28	3.33	84.9	266.6	.31	.42
15	00:03:45	13.8	10.45	3.08	86.0	265.5	.30	.41
16	00:04:00	14.0	10.65	3.22	86.4	264.9	.33	.42
17	00:04:15	14.3	11.18	3.27	87.2	275.5	.31	.42
18	00:04:30	14.5	10.63	3.29	83.8	272.9	.32	.44
19	00:04:45	14.8	10.43	3.31	81.6	265.9	.34	.45
20	00:05:00	15.0	10.65	3.26	80.1	257.4	.32	.44
21	00:05:15	15.3	9.33	3.14	80.0	249.2	.34	.45
22	00:05:30	15.5	10.30	3.31	79.4	256.6	.33	.45
23	00:05:45	15.8	10.18	3.08	80.9	254.6	.33	.45
24	00:06:00	16.0	10.40	3.31	80.2	258.7	.34	.45
25	00:06:15	16.3	10.27	3.27	80.5	264.3	.34	.45
26	00:06:30	16.5	10.3	3.33	79.7	262.5	.34	.45
27	00:06:45	16.8	10.53	3.42	78.2	258.4	.35	.47
28	00:07:00	17.0	9.95	3.26	78.2	253.5	.34	.45
29	00:07:15	17.3	10.27	3.34	80.8	262.1	.33	.44
30	00:07:30	17.5	9.90	3.03	82.5	260.0	.32	.44
31	00:07:45	17.8	9.80	3.16	81.3	257.9	.33	.45
32	00:08:00	18.0	9.43	3.15	79.3	252.2	.34	.48
33	00:08:15	18.3	9.38	3.20	79.5	251.6	.32	.44
34	00:08:30	18.5	9.50	3.19	79.4	252.1	.33	.45
35	00:08:45	18.8	9.08	3.05	79.7	244.1	.32	.44
36	00:09:00	19.0	9.15	3.03	80.4	244.2	.32	.44
37	00:09:15	19.3	9.55	3.16	79.3	241.7	.33	.45
38	00:09:30	19.5	9.93	3.06	80.5	243.1	.32	.44
39	00:09:45	19.8	8.73	3.07	79.2	237.7	.34	.46
40	00:10:00	20.0	8.75	3.00	78.1	235.2	.33	.45
41	00:10:15	20.3	8.48	2.95	78.1	233.3	.34	.45
42	00:10:30	20.5	8.73	3.05	78.2	229.4	.34	.45
43	00:10:45	20.8	8.93	3.15	77.4	233.4	.35	.46
44	00:11:00	21.0	8.75	3.05	76.9	235.7	.35	.46

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
45	00:11:15	21.3	9.20	2.87	78.1	230.7	.33	.45
46	00:11:30	21.5	9.03	3.16	78.9	234.2	.36	.46
47	00:11:45	21.8	10.25	3.00	79.9	239.7	.34	.44
48	00:12:00	22.0	9.05	3.18	79.3	240.8	.34	.46
49	00:12:15	22.3	8.68	3.06	77.8	236.2	.35	.46
50	00:12:30	22.5	9.08	3.20	76.4	234.9	.37	.47
51	00:12:45	22.8	9.08	3.17	76.9	240.7	.36	.46
52	00:13:00	23.0	9.08	3.12	77.2	242.9	.35	.45
53	00:13:15	23.3	9.23	3.04	80.6	242.4	.34	.44
54	00:13:30	23.5	10.25	3.04	85.2	239.8	.33	.44
55	00:13:45	23.8	8.85	3.12	80.7	233.7	.36	.45
56	00:14:00	24.0	9.25	3.10	77.4	232.2	.36	.47
57	00:14:15	24.3	8.80	3.05	78.2	235.7	.36	.45
58	00:14:30	24.5	8.88	3.16	77.8	235.3	.36	.46
59	00:14:45	24.8	8.53	3.06	76.8	229.5	.36	.46
60	00:15:00	25.0	8.45	3.15	75.3	228.9	.37	.47
61	00:15:15	25.3	8.60	3.14	75.0	227.2	.36	.46
62	00:15:30	25.5	8.95	3.19	75.7	230.8	.36	.46
63	00:15:45	25.8	8.90	3.18	75.1	232.0	.37	.46
64	00:16:00	26.0	8.95	3.35	74.2	230.2	.37	.48
65	00:16:15	26.3	9.08	3.09	72.6	221.7	.38	.46
66	00:16:30	26.5	8.66	3.07	74.7	219.7	.37	.46
67	00:16:45	26.8	8.13	2.95	74.1	213.7	.37	.46
68	00:17:00	27.0	8.75	3.03	76.3	218.8	.35	.47
69	00:17:15	27.3	9.13	3.20	76.3	225.9	.37	.46
70	00:17:30	27.5	10.15	3.18	77.7	235.7	.35	.44
71	00:17:45	27.8	10.38	3.31	82.1	251.5	.35	.42
72	00:18:00	28.0	10.40	3.39	81.5	263.4	.35	.43
73	00:18:15	28.3	10.45	3.37	80.4	265.4	.36	.44
74	00:18:30	28.5	9.38	3.24	76.9	243.9	.37	.48
75	00:18:45	28.8	9.83	3.23	76.4	242.1	.36	.45
76	00:19:00	29.0	11.33	3.29	77.3	245.7	.36	.43
77	00:19:15	29.3	10.15	3.44	78.0	252.1	.37	.44
78	00:19:30	29.5	11.48	3.39	80.4	254.7	.35	.41
79	00:19:45	29.8	11.30	3.66	80.6	268.2	.36	.42
80	00:20:00	30.0	11.63	3.34	81.4	262.4	.35	.43
81	00:20:15	30.3	11.63	3.38	84.1	262.3	.34	.41
82	00:20:30	30.5	11.43	3.55	83.1	268.8	.36	.42
83	00:20:45	30.8	11.53	3.53	81.9	272.8	.36	.42
84	00:21:00	31.0	11.60	3.41	80.3	267.1	.37	.41
85	00:21:15	31.3	11.48	3.43	78.8	248.4	.38	.44
86	00:21:30	31.5	11.85	3.18	80.6	239.1	.35	.42

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
87	00:21:45	31.8	10.33	3.40	78.5	240.5	.37	.44
88	00:22:00	32.0	11.15	3.49	76.6	248.7	.37	.44
89	00:22:15	32.3	9.52	3.28	76.6	245.3	.37	.43
90	00:22:30	32.5	10.73	3.38	77.7	245.6	.37	.43
91	00:22:45	32.8	11.55	3.14	82.8	243.8	.34	.40
92	00:23:00	33.0	12.00	3.18	90.4	246.5	.35	.41
93	00:23:15	33.3	13.07	3.36	88.7	257.0	.38	.42
94	00:23:30	33.5	13.63	3.39	85.4	255.4	.40	.42
95	00:23:45	33.8	14.55	3.63	86.8	264.5	.40	.41
96	00:24:00	34.0	15.85	3.97	85.2	279.5	.39	.41
97	00:24:15	34.3	13.00	3.65	80.8	275.0	.39	.43
98	00:24:30	34.5	12.65	3.65	79.3	274.6	.38	.42
99	00:24:45	34.8	14.55	3.71	78.9	275.1	.40	.40
100	00:25:00	35.0	12.28	3.54	77.5	267.3	.39	.43
101	00:25:15	35.3	14.08	3.58	79.3	268.2	.39	.40
102	00:25:30	35.5	13.98	3.72	77.4	266.8	.42	.42
103	00:25:45	35.8	13.75	3.66	75.9	261.0	.40	.43
104	00:26:00	36.0	12.27	3.56	76.5	258.0	.38	.42
105	00:26:15	36.3	14.75	3.57	82.4	261.1	.35	.40
106	00:26:30	36.5	11.82	3.65	80.7	261.2	.38	.42
107	00:26:45	36.8	12.03	3.52	80.9	265.3	.35	.40
108	00:27:00	37.0	12.00	3.68	81.7	254.1	.38	.43
109	00:27:15	37.3	10.77	3.42	77.2	249.5	.38	.45
110	00:27:30	37.5	9.77	3.32	74.8	241.1	.38	.46
111	00:27:45	37.8	9.40	3.14	75.2	237.6	.38	.45
112	00:28:00	38.0	9.20	3.12	73.2	224.2	.38	.48
113	00:28:15	38.3	9.28	3.20	72.6	219.2	.38	.47
114	00:28:30	38.5	9.73	3.34	72.2	225.0	.39	.47
115	00:28:45	38.8	10.28	3.38	72.7	233.8	.38	.47
116	00:29:00	39.0	9.80	3.33	73.4	238.8	.38	.48
117	00:29:15	39.3	10.15	3.54	70.8	231.2	.38	.50
118	00:29:30	39.5	10.92	3.29	72.1	227.3	.40	.45
119	00:29:45	39.8	9.88	3.37	72.3	233.7	.39	.47
120	00:30:00	40.0	10.10	3.41	72.4	239.0	.39	.46
1	00:00:15	40.3	6.43	2.61	77.4	184.2	.38	.49
2	00:00:30	40.5	6.18	2.46	71.7	180.1	.40	.50
3	00:00:45	40.8	6.35	2.78	68.7	177.6	.41	.52
4	00:01:00	41.0	6.35	2.77	66.9	178.9	.41	.53
5	00:01:15	41.3	6.95	2.86	67.2	184.6	.40	.52
6	00:01:30	41.5	8.68	2.89	69.7	186.5	.40	.48
7	00:01:45	41.8	7.13	2.95	69.3	194.9	.40	.49
8	00:02:00	42.0	7.33	2.96	69.5	201.6	.40	.49

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
9	00:02:15	42.3	7.25	2.96	69.4	201.5	.40	.50
10	00:02:30	42.5	6.60	2.80	67.6	185.8	.41	.51
11	00:02:45	42.8	6.98	2.86	68.3	193.0	.39	.50
12	00:03:00	43.0	7.10	2.84	70.6	195.5	.38	.49
13	00:03:15	43.3	7.15	2.88	69.8	195.9	.40	.50
14	00:03:30	43.5	6.83	2.72	69.5	183.7	.39	.51
15	00:03:45	43.8	6.53	2.70	68.1	181.0	.39	.52
16	00:04:00	44.0	7.40	2.95	67.6	185.4	.39	.53
17	00:04:15	44.3	8.28	3.04	68.4	193.5	.38	.49
18	00:04:30	44.5	7.52	2.83	70.5	197.7	.38	.49
19	00:04:45	44.8	7.05	2.87	68.5	198.5	.41	.52
20	00:05:00	45.0	7.23	2.83	67.3	184.1	.39	.50
21	00:05:15	45.3	7.65	2.83	69.2	197.0	.37	.49
22	00:05:30	45.5	6.63	2.65	70.4	187.7	.37	.50
23	00:05:45	45.8	6.70	2.76	69.1	186.9	.38	.52
24	00:06:00	46.0	7.28	2.62	70.5	183.8	.35	.50
25	00:06:15	46.3	7.48	2.96	69.8	184.3	.39	.50
26	00:06:30	46.5	7.20	2.90	66.9	181.6	.38	.54
27	00:06:45	46.8	7.48	2.91	68.9	194.2	.37	.49
28	00:07:00	47.0	7.73	2.99	70.8	197.3	.37	.49
29	00:07:15	47.3	7.30	2.86	71.5	200.6	.37	.49
30	00:07:30	47.5	7.48	2.91	71.4	202.7	.37	.49
31	00:07:45	47.8	7.47	2.90	70.6	201.2	.37	.49
32	00:08:00	48.0	7.33	2.89	71.1	199.9	.37	.49
33	00:08:15	48.3	7.43	2.77	72.6	199.6	.38	.47
34	00:08:30	48.5	7.38	2.75	71.9	190.7	.36	.48
35	00:08:45	48.8	7.38	2.80	73.6	196.6	.36	.48
36	00:09:00	49.0	7.78	2.82	74.2	201.3	.36	.48
37	00:09:15	49.3	7.38	2.63	75.7	199.6	.34	.48
38	00:09:30	49.5	6.50	2.68	73.7	189.7	.37	.51
39	00:09:45	49.8	7.58	2.86	71.6	193.2	.37	.50
40	00:10:00	50.0	7.80	3.03	71.5	204.6	.36	.50
41	00:10:15	50.3	7.85	3.07	70.8	206.5	.36	.50
42	00:10:30	50.5	8.30	3.11	71.3	209.0	.36	.50
43	00:10:45	50.8	8.23	3.13	72.3	215.7	.36	.49
44	00:11:00	51.0	8.03	2.83	73.3	216.0	.36	.49
45	00:11:15	51.3	8.20	2.99	74.0	216.1	.37	.50
46	00:11:30	51.5	8.02	2.99	73.1	215.6	.38	.50
47	00:11:45	51.8	8.23	3.17	70.5	206.9	.38	.51
48	00:12:00	52.0	8.90	3.12	71.7	218.7	.37	.49
49	00:12:15	52.3	9.67	3.00	74.2	222.9	.36	.46
50	00:12:30	52.5	8.67	2.91	76.9	224.5	.38	.44

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
51	00:12:45	52.8	7.33	2.80	75.7	207.0	.35	.47
52	00:13:00	53.0	8.50	2.96	75.0	210.6	.35	.47
53	00:13:15	53.3	8.38	2.91	76.9	219.7	.36	.45
54	00:13:30	53.5	8.35	2.92	76.3	219.0	.37	.46
55	00:13:45	53.8	8.13	2.68	79.5	213.9	.37	.45
56	00:14:00	54.0	9.25	2.58	81.7	204.3	.33	.44
57	00:14:15	54.3	6.93	2.71	81.9	196.0	.35	.47
58	00:14:30	54.5	7.40	2.92	75.6	197.6	.37	.48
59	00:14:45	54.8	9.07	2.84	81.3	208.1	.34	.45
60	00:15:00	55.0	7.85	2.88	77.7	213.6	.36	.47
61	00:15:15	55.3	8.10	2.94	76.6	212.6	.36	.47
62	00:15:30	55.5	8.00	2.93	74.8	207.8	.36	.48
63	00:15:45	55.8	7.68	2.86	74.0	203.3	.36	.48
64	00:16:00	56.0	8.25	2.82	73.8	202.3	.35	.46
65	00:16:15	56.3	8.20	2.94	75.0	207.9	.35	.47
66	00:16:30	56.5	8.35	3.00	75.0	212.1	.35	.47
67	00:16:45	56.8	7.70	2.79	74.5	206.2	.35	.48
68	00:17:00	57.0	7.93	2.87	73.8	205.3	.35	.47
69	00:17:15	57.3	7.77	2.91	73.4	207.5	.35	.48
70	00:17:30	57.5	8.02	2.79	73.6	203.0	.35	.47
71	00:17:45	57.8	7.30	2.68	74.3	191.1	.37	.48
72	00:18:00	58.0	7.98	2.87	72.6	194.7	.36	.49
73	00:18:15	58.3	7.90	2.83	71.6	199.2	.37	.49
74	00:18:30	58.5	7.63	2.85	70.9	194.7	.36	.50
75	00:18:45	58.8	8.52	2.74	71.1	193.5	.35	.48
76	00:19:00	59.0	8.25	2.90	70.3	196.5	.35	.50
77	00:19:15	59.3	9.30	2.56	78.6	202.1	.31	.44
78	00:19:30	59.5	8.23	3.04	75.3	201.1	.35	.48
79	00:19:45	59.8	8.63	2.80	76.4	208.3	.32	.45
80	00:20:00	60.0	7.55	2.80	77.1	207.3	.35	.46
81	00:20:15	60.3	7.43	2.92	74.1	207.0	.37	.47
82	00:20:30	60.5	7.13	2.69	73.6	196.3	.36	.47
83	00:20:45	60.8	7.30	2.78	72.0	191.3	.35	.49
84	00:21:00	61.0	7.15	2.65	72.3	186.9	.36	.48
85	00:21:15	61.3	6.83	2.59	71.9	186.9	.36	.49
86	00:21:30	61.5	6.60	2.60	72.2	181.2	.36	.48
87	00:21:45	61.8	7.30	2.55	73.4	182.1	.34	.47
88	00:22:00	62.0	7.18	2.81	73.5	183.3	.36	.49
89	00:22:15	62.3	8.20	2.73	71.7	191.2	.35	.49
90	00:22:30	62.5	7.68	2.90	73.5	204.6	.35	.48
91	00:22:45	62.8	7.90	3.06	72.1	206.8	.36	.49
92	00:23:00	63.0	7.88	2.92	71.7	206.1	.35	.48

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
93	00:23:15	63.3	7.78	2.91	73.3	208.1	.36	.48
94	00:23:30	63.5	7.33	2.68	74.1	202.2	.34	.46
95	00:23:45	63.8	7.57	2.87	74.1	201.3	.35	.47
96	00:24:00	64.0	7.45	2.66	75.1	198.8	.35	.46
97	00:24:15	64.3	7.02	2.67	74.1	195.3	.37	.47
98	00:24:30	64.5	7.40	2.71	71.6	187.9	.36	.49
99	00:24:45	64.8	8.75	2.31	84.5	187.0	.32	.43
100	00:25:00	65.0	8.15	2.84	86.2	198.3	.36	.46
101	00:25:15	65.3	8.98	2.93	82.6	213.5	.35	.46
102	00:25:30	65.5	9.53	2.83	80.3	218.2	.34	.45
103	00:25:45	65.8	9.63	3.02	84.6	238.1	.35	.46
104	00:26:00	66.0	9.60	3.14	80.5	234.9	.37	.46
105	00:26:15	66.3	9.63	3.13	77.2	237.1	.37	.46
106	00:26:30	66.5	10.73	3.24	75.9	238.3	.37	.45
107	00:26:45	66.8	9.30	3.18	75.5	236.7	.36	.45
108	00:27:00	67.0	8.85	3.12	74.9	231.9	.37	.46
109	00:27:15	67.3	8.20	2.98	73.8	219.8	.37	.49
110	00:27:30	67.5	8.52	3.09	71.7	207.5	.36	.50
111	00:27:45	67.8	8.15	2.92	72.5	208.8	.36	.47
112	00:28:00	68.0	8.50	3.03	74.5	217.3	.35	.46
113	00:28:15	68.3	8.53	2.96	75.5	222.9	.36	.46
114	00:28:30	63.5	7.85	2.84	74.2	214.6	.36	.47
115	00:28:45	68.8	7.53	2.74	73.6	200.3	.37	.47
116	00:29:00	69.0	7.50	2.84	72.7	200.0	.38	.48
117	00:29:15	69.3	7.60	2.88	71.0	198.6	.38	.49
118	00:29:30	69.5	7.30	2.79	69.5	193.9	.38	.50
119	00:29:45	69.8	7.95	3.00	69.2	194.9	.38	.51
120	00:30:00	70.0	8.15	2.99	69.5	198.8	.37	.49

Control-Period: 0.0 - 10.0 (minutes)
Exposure-Period: 10.3 - 40.0 (minutes)
Recovery-Period: 40.3 - 70.0 (minutes)

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
1	00:00:15	.3	12.55	3.52	88.5	302.0	.25	.41
2	00:00:30	.5	11.80	3.62	89.0	297.5	.27	.42
3	00:00:45	.8	12.28	3.70	89.7	303.3	.26	.41
4	00:01:00	1.0	13.35	3.77	91.5	311.2	.26	.41
5	00:01:15	1.3	13.30	4.02	90.2	318.7	.26	.41
6	00:01:30	1.5	13.25	3.97	91.5	325.9	.25	.40
7	00:01:45	1.8	15.23	4.0	92.4	324.9	.25	.39
8	00:02:00	2.0	12.85	3.	92.7	325.9	.26	.41
9	00:02:15	2.3	13.33	4.	91.9	328.0	.26	.41
10	00:02:30	2.5	13.50	4.11	91.7	327.6	.26	.40
11	00:02:45	2.8	13.75	4.10	92.2	328.6	.25	.40
12	00:03:00	3.0	14.15	3.85	96.3	340.6	.24	.37
13	00:03:15	3.3	14.33	3.98	96.8	336.0	.25	.41
14	00:03:30	3.5	14.15	3.77	96.5	331.8	.25	.40
15	00:03:45	3.8	13.68	3.67	100.2	331.7	.23	.38
16	00:04:00	4.0	14.63	3.70	102.1	326.7	.23	.39
17	00:04:15	4.3	13.08	4.11	97.2	336.8	.25	.38
18	00:04:30	4.5	14.53	3.88	101.7	338.5	.23	.37
19	00:04:45	4.8	12.52	3.88	98.2	336.5	.25	.39
20	00:05:00	5.0	12.35	3.81	95.4	328.2	.25	.40
21	00:05:15	5.3	13.48	3.95	94.6	328.0	.25	.39
22	00:05:30	5.5	13.52	3.93	95.1	326.8	.25	.39
23	00:05:45	5.8	12.60	3.74	94.6	316.7	.25	.39
24	00:06:00	6.0	13.05	3.70	95.5	317.7	.24	.38
25	00:06:15	6.3	13.25	3.69	96.3	314.4	.25	.38
26	00:06:30	6.5	14.85	3.63	98.4	323.3	.24	.36
27	00:06:45	6.8	12.80	3.78	99.1	315.4	.26	.40
28	00:07:00	7.0	13.05	3.64	94.4	304.5	.25	.40
29	00:07:15	7.3	13.33	3.80	95.1	306.2	.25	.38
30	00:07:30	7.5	14.15	3.57	96.6	310.1	.25	.38
31	00:07:45	7.8	12.85	3.60	96.1	307.3	.26	.39
32	00:08:00	8.0	13.33	3.65	95.6	310.8	.25	.38
33	00:08:15	8.3	13.23	3.60	96.6	312.6	.25	.38
34	00:08:30	8.5	13.60	3.55	97.2	315.0	.25	.36
35	00:08:45	8.8	13.48	3.49	101.0	314.8	.25	.37
36	00:09:00	9.0	13.18	3.71	99.2	312.8	.26	.38
37	00:09:15	9.3	13.35	3.54	100.7	316.0	.25	.37
38	00:09:30	9.5	12.30	3.64	97.2	307.3	.26	.39
39	00:09:45	9.8	12.27	3.48	97.3	295.8	.26	.39
40	00:10:00	10.0	12.50	3.77	93.9	305.2	.27	.38
1	00:00:15	10.3	11.63	3.22	119.5	360.0	.21	.35
2	00:00:30	10.5	11.18	3.16	108.8	326.8	.22	.36

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T5039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
3	00:00:45	10.8	12.10	3.27	103.5	311.3	.25	.37
4	00:01:00	11.0	12.43	3.40	100.1	299.4	.25	.36
5	00:01:15	11.3	12.45	3.47	101.7	308.3	.26	.36
6	00:01:30	11.5	13.13	3.63	98.3	314.7	.26	.37
7	00:01:45	11.8	12.90	3.77	95.3	316.0	.28	.37
8	00:02:00	12.0	13.38	3.95	93.2	317.9	.29	.37
9	00:02:15	12.3	13.48	3.98	91.9	316.2	.29	.38
10	00:02:30	12.5	13.78	4.11	90.7	314.2	.29	.38
11	00:02:45	12.8	13.80	4.08	91.7	314.9	.29	.38
12	00:03:00	13.0	13.40	3.91	92.3	322.0	.28	.37
13	00:03:15	13.3	13.75	3.95	94.7	326.1	.28	.36
14	00:03:30	13.5	13.70	4.01	94.0	326.2	.28	.37
15	00:03:45	13.8	13.60	3.98	92.2	322.2	.29	.37
16	00:04:00	14.0	14.95	3.93	93.0	325.3	.29	.37
17	00:04:15	14.3	14.08	4.08	90.0	317.2	.32	.39
18	00:04:30	14.5	15.00	3.99	88.5	299.0	.32	.38
19	00:04:45	14.8	13.85	3.92	90.2	308.5	.32	.37
20	00:05:00	15.0	13.30	3.83	91.1	306.0	.34	.39
21	00:05:15	15.3	15.15	3.98	87.5	294.8	.37	.39
22	00:05:30	15.5	15.18	3.98	86.8	294.1	.34	.38
23	00:05:45	15.8	14.02	3.93	87.9	301.8	.35	.38
24	00:06:00	16.0	14.75	4.01	86.3	296.0	.37	.38
25	00:06:15	16.3	15.05	3.56	91.0	293.9	.30	.33
26	00:06:30	16.5	14.60	4.26	92.5	301.9	.34	.38
27	00:06:45	16.8	13.90	4.12	88.6	301.6	.34	.38
28	00:07:00	17.0	13.18	3.75	91.1	292.0	.31	.37
29	00:07:15	17.3	13.50	4.09	88.1	294.4	.33	.39
30	00:07:30	17.5	13.08	4.08	85.8	292.6	.36	.40
31	00:07:45	17.8	14.70	4.11	85.8	288.4	.39	.38
32	00:08:00	18.0	13.73	4.05	85.8	277.2	.38	.39
33	00:08:15	18.3	17.13	4.30	85.4	277.9	.44	.37
34	00:08:30	18.5	16.38	4.35	84.6	279.2	.44	.37
35	00:08:45	18.8	17.00	4.39	84.9	282.6	.44	.36
36	00:09:00	19.0	15.88	4.17	84.4	279.4	.43	.37
37	00:09:15	19.3	13.50	4.16	83.8	264.6	.45	.39
38	00:09:30	19.5	15.93	4.37	81.5	259.7	.47	.38
39	00:09:45	19.8	17.35	4.48	79.7	259.0	.50	.39
40	00:10:00	20.0	14.43	4.40	79.5	254.9	.51	.38
41	00:10:15	20.3	17.95	4.13	80.8	256.9	.48	.36
42	00:10:30	20.5	14.40	4.55	80.5	255.1	.54	.42
43	00:10:45	20.8	13.90	4.61	80.1	259.3	.54	.42
44	00:11:00	21.0	13.93	4.53	78.8	250.0	.58	.44

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
45	00:11:15	21.3	16.88	4.94	77.4	241.4	.71	.39
46	00:11:30	21.5	18.83	4.75	79.0	243.4	.69	.37
47	00:11:45	21.8	14.95	4.41	79.3	240.3	.45	.45
48	00:12:00	22.0	13.45	4.60	77.0	238.4	.48	.51
49	00:12:15	22.3	12.48	4.27	76.6	241.4	.44	.49
50	00:12:30	22.5	11.75	3.84	78.7	251.6	.35	.44
51	00:12:45	22.8	9.25	2.90	89.5	265.5	.25	.40
52	00:13:00	23.0	9.68	2.78	91.9	256.1	.28	.37
53	00:13:15	23.3	11.05	2.98	92.2	248.0	.27	.38
54	00:13:30	23.5	9.53	2.97	91.9	249.3	.27	.40
55	00:13:45	23.8	8.53	3.02	91.0	246.8	.28	.45
56	00:14:00	24.0	8.65	3.19	84.3	244.1	.31	.46
57	00:14:15	24.3	9.27	3.28	82.0	239.8	.33	.46
58	00:14:30	24.5	10.13	3.36	81.0	233.5	.35	.46
59	00:14:45	24.8	9.78	3.47	78.7	233.6	.38	.46
60	00:15:00	25.0	10.95	3.62	76.4	230.1	.40	.47
61	00:15:15	25.3	10.93	3.58	79.3	239.0	.38	.44
62	00:15:30	25.5	11.43	3.72	78.7	240.6	.38	.45
63	00:15:45	25.8	10.70	3.58	79.8	243.9	.38	.44
64	00:16:00	26.0	11.35	3.68	79.8	249.4	.37	.42
65	00:16:15	26.3	10.70	3.74	81.0	248.6	.38	.43
66	00:16:30	26.5	11.58	3.75	79.5	250.1	.36	.44
67	00:16:45	26.8	11.40	3.71	80.6	253.6	.37	.43
68	00:17:00	27.0	11.10	3.63	82.4	251.4	.37	.42
69	00:17:15	27.3	12.88	3.67	82.4	251.0	.36	.42
70	00:17:30	27.5	12.38	3.89	80.6	248.9	.39	.43
71	00:17:45	27.8	12.45	3.46	82.4	252.8	.35	.40
72	00:18:00	28.0	11.03	3.82	82.1	247.2	.37	.43
73	00:18:15	28.3	10.65	3.57	82.7	253.7	.35	.42
74	00:18:30	28.5	12.25	3.86	82.2	257.0	.39	.42
75	00:18:45	28.8	12.15	3.75	80.4	258.7	.39	.41
76	00:19:00	29.0	11.45	3.82	78.5	249.8	.38	.43
77	00:19:15	29.3	11.15	3.89	76.1	245.7	.41	.44
78	00:19:30	29.5	13.05	3.94	76.6	247.5	.40	.41
79	00:19:45	29.8	12.43	3.76	78.3	249.5	.40	.42
80	00:20:00	30.0	12.35	3.83	77.2	244.5	.40	.43
81	00:20:15	30.3	12.63	3.79	76.1	245.4	.40	.41
82	00:20:30	30.5	11.60	3.89	75.4	237.4	.38	.44
83	00:20:45	30.8	11.00	3.77	77.4	241.4	.38	.43
84	00:21:00	31.0	13.23	3.85	76.1	239.4	.42	.41
85	00:21:15	31.3	11.45	3.56	77.4	240.2	.38	.41
86	00:21:30	31.5	11.33	3.76	76.3	238.2	.40	.44

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
87	00:21:45	31.8	13.00	3.76	75.1	229.5	.43	.43
88	00:22:00	32.0	11.98	3.81	76.5	230.0	.43	.43
89	00:22:15	32.3	12.35	3.80	76.6	237.4	.42	.41
90	00:22:30	32.5	12.05	3.60	78.9	236.7	.42	.39
91	00:22:45	32.8	12.40	3.62	79.1	225.8	.44	.42
92	00:23:00	33.0	12.15	3.91	72.7	216.7	.48	.44
93	00:23:15	33.3	12.33	3.88	73.0	212.8	.46	.42
94	00:23:30	33.5	11.83	3.67	78.2	226.0	.44	.42
95	00:23:45	33.8	11.40	3.79	74.4	220.3	.48	.45
96	00:24:00	34.0	12.23	3.92	74.0	217.6	.49	.43
97	00:24:15	34.3	12.05	3.61	76.7	220.6	.48	.42
98	00:24:30	34.5	11.35	4.03	75.3	216.7	.50	.45
99	00:24:45	34.8	12.20	3.89	73.3	220.0	.48	.44
100	00:25:00	35.0	11.92	4.02	72.0	221.5	.51	.49
101	00:25:15	35.3	12.90	4.17	71.8	221.1	.52	.44
102	00:25:30	35.5	12.93	4.06	70.3	213.8	.55	.44
103	00:25:45	35.8	12.55	4.28	69.0	205.7	.55	.46
104	00:26:00	36.0	13.18	4.18	68.1	204.7	.56	.47
105	00:26:15	36.3	11.75	4.06	68.7	206.9	.55	.46
106	00:26:30	36.5	12.15	3.78	72.6	211.3	.51	.44
107	00:26:45	36.8	11.45	4.05	71.0	211.2	.54	.46
108	00:27:00	37.0	11.48	3.91	71.3	215.5	.49	.46
109	00:27:15	37.3	10.23	3.71	70.3	214.0	.46	.48
110	00:27:30	37.5	9.68	3.77	70.7	216.8	.45	.48
111	00:27:45	37.8	12.55	3.66	73.5	222.6	.44	.45
112	00:28:00	38.0	10.83	3.74	69.9	206.9	.48	.48
113	00:28:15	38.3	12.18	3.91	68.5	203.2	.48	.46
114	00:28:30	38.5	10.57	3.70	69.1	204.6	.48	.47
115	00:28:45	38.8	10.40	3.56	71.6	209.1	.41	.45
116	00:29:00	39.0	9.25	3.52	71.6	212.8	.44	.47
117	00:29:15	39.3	9.05	3.48	70.6	209.2	.44	.49
118	00:29:30	39.5	11.93	3.58	70.6	208.8	.46	.45
119	00:29:45	39.8	11.83	3.79	69.6	210.6	.47	.47
120	00:30:00	40.0	11.50	3.68	70.1	212.9	.46	.45
1	00:00:15	40.3	5.88	2.67	76.9	178.4	.40	.51
2	00:00:30	40.5	6.25	2.92	72.8	176.1	.43	.54
3	00:00:45	40.8	5.68	2.74	67.9	171.5	.44	.55
4	00:01:00	41.0	6.18	2.76	65.9	159.8	.45	.54
5	00:01:15	41.3	6.43	2.79	68.2	164.6	.42	.52
6	00:01:30	41.5	6.53	2.79	69.0	169.3	.43	.52
7	00:01:45	41.8	6.32	2.84	67.6	167.2	.43	.53
8	00:02:00	42.0	6.95	2.96	67.8	169.0	.43	.50

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
9	00:02:15	42.3	7.88	3.15	68.6	180.1	.43	.[illegible]
10	00:02:30	42.5	7.43	3.12	68.3	184.7	.44	.[illegible]
11	00:02:45	42.8	8.78	3.22	69.0	189.7	.43	.49
12	00:03:00	43.0	8.43	3.17	69.3	189.7	.42	.47
13	00:03:15	43.3	8.60	2.82	68.8	181.2	.44	.50
14	00:03:30	43.5	7.28	2.94	67.7	171.0	.42	.48
15	00:03:45	43.8	7.60	2.99	68.8	175.6	.42	.47
16	00:04:00	44.0	9.20	3.27	68.7	181.4	.44	.48
17	00:04:15	44.3	8.75	3.41	68.8	195.2	.42	.49
18	00:04:30	44.5	9.70	3.31	69.2	199.1	.41	.49
19	00:04:45	44.8	8.88	3.09	70.4	198.0	.40	.46
20	00:05:00	45.0	9.00	3.32	71.2	202.8	.41	.49
21	00:05:15	45.3	9.73	3.30	71.4	208.6	.42	.45
22	00:05:30	45.5	9.25	3.37	72.7	209.3	.40	.46
23	00:05:45	45.8	9.48	3.43	73.2	204.9	.44	.46
24	00:06:00	46.0	10.05	3.50	72.1	207.1	.44	.44
25	00:06:15	46.3	9.88	3.34	72.1	204.9	.45	.43
26	00:06:30	46.5	10.90	3.25	72.7	205.3	.41	.44
27	00:06:45	46.8	8.15	3.01	73.2	201.0	.40	.45
28	00:07:00	47.0	9.53	3.72	70.1	195.1	.44	.49
29	00:07:15	47.3	9.88	3.44	69.9	205.0	.43	.45
30	00:07:30	47.5	8.70	3.32	71.3	199.3	.45	.46
31	00:07:45	47.8	10.88	3.39	72.1	206.6	.41	.44
32	00:08:00	48.0	10.80	3.51	75.6	216.5	.42	.44
33	00:08:15	48.3	9.42	3.24	75.4	212.6	.42	.45
34	00:08:30	48.5	9.88	3.55	73.6	213.0	.42	.47
35	00:08:45	48.8	8.93	3.28	71.6	206.1	.43	.50
36	00:09:00	49.0	9.70	3.35	71.1	203.4	.42	.45
37	00:09:15	49.3	10.42	3.52	71.7	215.7	.42	.44
38	00:09:30	49.5	9.48	3.20	72.4	215.0	.40	.45
39	00:09:45	49.8	9.65	3.31	73.4	211.8	.40	.45
40	00:10:00	50.0	9.90	3.36	71.6	212.9	.41	.46
41	00:10:15	50.3	11.10	3.63	71.0	214.2	.43	.45
42	00:10:30	50.5	10.38	3.17	72.4	216.5	.38	.44
43	00:10:45	50.8	9.58	3.36	74.9	224.6	.35	.45
44	00:11:00	51.0	9.43	3.22	75.0	226.3	.39	.45
45	00:11:15	51.3	9.20	3.34	74.2	219.9	.39	.45
46	00:11:30	51.5	9.25	3.41	74.1	218.4	.40	.47
47	00:11:45	51.8	9.30	3.19	75.4	220.6	.37	.43
48	00:12:00	52.0	9.03	3.26	76.6	210.5	.40	.46
49	00:12:15	52.3	9.10	3.58	74.2	209.9	.41	.48
50	00:12:30	52.5	9.50	3.20	77.2	215.7	.38	.45

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
51	00:12:45	52.8	10.80	3.50	77.7	219.0	.39	.47
52	00:13:00	53.0	9.88	3.52	77.8	219.2	.39	.47
53	00:13:15	53.3	11.73	3.48	80.2	224.6	.38	.46
54	00:13:30	53.5	10.95	3.82	77.8	226.0	.40	.48
55	00:13:45	53.8	10.67	3.64	78.3	237.2	.37	.44
56	00:14:00	54.0	10.23	3.56	76.9	239.0	.38	.47
57	00:14:15	54.3	10.48	3.27	82.9	226.7	.36	.44
58	00:14:30	54.5	10.20	3.42	81.6	238.4	.36	.44
59	00:14:45	54.8	9.60	3.21	82.4	239.8	.36	.44
60	00:15:00	55.0	9.90	3.33	80.6	234.7	.34	.46
61	00:15:15	55.3	9.10	2.99	80.4	228.2	.35	.46
62	00:15:30	55.5	9.13	3.28	77.1	227.2	.34	.49
63	00:15:45	55.8	8.48	2.91	78.1	226.5	.33	.46
64	00:16:00	56.0	9.85	3.23	80.0	224.1	.36	.47
65	00:16:15	56.3	9.67	3.08	77.6	226.3	.36	.47
66	00:16:30	56.5	9.73	3.14	84.4	228.3	.34	.46
67	00:16:45	56.8	10.17	3.42	81.8	243.3	.35	.46
68	00:17:00	57.0	11.57	3.40	81.9	249.1	.34	.45
69	00:17:15	57.3	11.85	3.76	81.3	245.4	.37	.48
70	00:17:30	57.5	12.18	3.66	78.1	247.8	.36	.46
71	00:17:45	57.8	12.83	3.84	78.5	252.2	.38	.43
72	00:18:00	58.0	11.76	3.39	80.7	254.1	.35	.42
73	00:18:15	58.3	11.48	3.52	82.2	254.0	.36	.45
74	00:18:30	58.5	12.05	3.69	77.8	252.5	.36	.47
75	00:18:45	58.8	12.30	3.64	79.7	260.8	.34	.42
76	00:19:00	59.0	11.75	3.43	83.5	260.8	.32	.41
77	00:19:15	59.3	10.75	3.70	79.9	245.4	.36	.48
78	00:19:30	59.5	11.40	3.42	79.1	250.6	.32	.44
79	00:19:45	59.8	11.42	3.36	84.0	246.3	.33	.43
80	00:20:00	60.0	10.98	3.24	85.9	243.4	.32	.43
81	00:20:15	60.3	10.95	3.40	83.8	248.4	.32	.44
82	00:20:30	60.5	11.00	3.74	80.1	247.5	.33	.46
83	00:20:45	60.8	9.95	3.40	76.6	235.5	.33	.48
84	00:21:00	61.0	9.75	3.23	77.1	228.5	.32	.46
85	00:21:15	61.3	9.93	3.05	82.9	230.9	.32	.43
86	00:21:30	61.5	9.23	3.22	78.9	225.0	.35	.46
87	00:21:45	61.8	9.53	3.34	73.7	215.2	.36	.49
88	00:22:00	62.0	9.23	3.26	73.7	219.0	.35	.47
89	00:22:15	62.3	9.15	3.28	73.2	222.1	.35	.48
90	00:22:30	62.5	8.75	3.15	72.6	220.1	.36	.48
91	00:22:45	62.8	8.93	3.18	73.1	218.4	.35	.46
92	00:23:00	63.0	9.10	3.25	74.0	212.0	.37	.49

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
93	00:23:15	63.3	8.68	3.06	72.9	209.3	.35	.48
94	00:23:30	63.5	9.08	2.99	76.0	218.1	.33	.45
95	00:23:45	63.8	9.43	3.24	75.2	222.9	.34	.47
96	00:24:00	64.0	9.40	3.12	79.2	218.6	.35	.46
97	00:24:15	64.3	8.80	3.27	74.6	210.3	.35	.50
98	00:24:30	64.5	9.23	3.20	75.0	223.5	.34	.45
99	00:24:45	64.8	8.95	3.13	76.2	222.3	.34	.46
100	00:25:00	65.0	11.00	3.16	81.0	221.4	.34	.45
101	00:25:15	65.3	9.93	3.28	79.9	226.7	.34	.45
102	00:25:30	65.5	10.58	3.52	77.9	240.1	.35	.47
103	00:25:45	65.8	11.20	3.54	77.3	248.3	.34	.45
104	00:26:00	66.0	10.80	3.76	76.5	242.1	.37	.48
105	00:26:15	66.3	10.75	3.51	76.2	237.8	.35	.45
106	00:26:30	66.5	10.58	3.32	76.1	236.7	.34	.45
107	00:26:45	66.8	11.35	3.39	78.7	251.1	.33	.44
108	00:27:00	67.0	10.70	3.47	78.2	251.9	.33	.44
109	00:27:15	67.3	10.23	3.41	76.9	247.6	.34	.47
110	00:27:30	67.5	10.52	3.35	78.3	241.9	.32	.45
111	00:27:45	67.8	10.70	3.54	77.9	239.7	.33	.46
112	00:28:00	68.0	10.52	3.47	78.5	244.2	.33	.44
113	00:28:15	68.3	10.30	3.51	76.9	242.3	.35	.46
114	00:28:30	68.5	10.49	3.26	79.4	248.0	.33	.44
115	00:28:45	68.8	10.30	3.33	79.4	250.7	.32	.44
116	00:29:00	69.0	10.75	3.31	81.4	243.8	.32	.44
117	00:29:15	69.3	11.38	3.60	78.2	250.7	.33	.46
118	00:29:30	69.5	10.75	3.46	78.0	242.0	.33	.44
119	00:29:45	69.8	12.38	3.24	82.6	251.5	.31	.42
120	00:30:00	70.0	10.98	2.97	97.9	260.1	.29	.41

Control-Period: 0.0 - 10.0 (minutes)
Exposure-Period: 10.3 - 40.0 (minutes)
Recovery-Period: 40.3 - 70.0 (minutes)

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
1	00:00:15	.3	9.40	3.21	88.3	268.8	.25	.42
2	00:00:30	.5	9.25	3.19	88.7	268.0	.25	.42
3	00:00:45	.8	9.68	3.28	90.4	273.3	.25	.41
4	00:01:00	1.0	9.90	3.36	90.9	281.8	.25	.40
5	00:01:15	1.3	10.05	3.36	91.6	282.8	.25	.41
6	00:01:30	1.5	10.30	3.46	92.3	286.2	.25	.40
7	00:01:45	1.8	10.13	3.28	92.8	288.6	.24	.40
8	00:02:00	2.0	10.35	3.29	95.1	293.4	.24	.39
9	00:02:15	2.3	10.13	3.35	94.9	288.7	.24	.40
10	00:02:30	2.5	10.08	3.14	97.5	292.3	.23	.38
11	00:02:45	2.8	10.40	3.32	95.3	285.7	.25	.40
12	00:03:00	3.0	9.75	3.09	94.6	280.2	.25	.40
13	00:03:15	3.3	10.03	3.07	95.6	279.1	.24	.38
14	00:03:30	3.5	10.23	3.12	96.9	281.1	.25	.38
15	00:03:45	3.8	10.63	3.03	99.6	290.4	.23	.36
16	00:04:00	4.0	9.80	3.02	99.1	284.4	.24	.38
17	00:04:15	4.3	10.13	3.11	96.4	278.9	.25	.39
18	00:04:30	4.5	9.93	2.92	97.4	275.4	.24	.39
19	00:04:45	4.8	9.78	3.12	95.4	271.8	.25	.39
20	00:05:00	5.0	10.75	3.01	95.4	271.6	.23	.40
21	00:05:15	5.3	9.40	3.10	94.2	263.8	.25	.41
22	00:05:30	5.5	9.45	3.14	91.8	268.8	.27	.40
23	00:05:45	5.8	10.33	3.07	94.4	275.4	.24	.38
24	00:06:00	6.0	10.42	3.13	95.5	277.7	.25	.39
25	00:06:15	6.3	10.40	3.43	91.7	276.8	.27	.42
26	00:06:30	6.5	10.58	3.22	91.8	275.8	.25	.40
27	00:06:45	6.8	10.75	3.14	93.1	275.5	.25	.38
28	00:07:00	7.0	10.23	3.07	99.9	280.8	.25	.39
29	00:07:15	7.3	10.88	3.07	98.6	281.7	.25	.38
30	00:07:30	7.5	10.98	3.10	99.6	286.4	.24	.38
31	00:07:45	7.8	9.92	2.97	98.6	281.6	.24	.38
32	00:08:00	8.0	10.30	2.85	101.6	277.5	.24	.38
33	00:08:15	8.3	9.93	3.14	96.7	279.2	.26	.40
34	00:08:30	8.5	9.00	3.05	89.4	262.5	.27	.44
35	00:08:45	8.8	9.70	3.26	84.0	255.6	.28	.45
36	00:09:00	9.0	10.05	3.30	84.2	258.8	.28	.43
37	00:09:15	9.3	10.38	3.30	84.2	264.9	.28	.43
38	00:09:30	9.5	9.13	3.18	83.4	258.5	.28	.45
39	00:09:45	9.8	9.08	3.04	85.3	251.5	.27	.44
40	00:10:00	10.0	10.30	3.29	84.5	255.3	.28	.45
41	00:10:15	10.3	10.05	3.32	84.0	259.9	.28	.44
42	00:10:30	10.5	10.03	3.26	85.8	266.8	.28	.43

LUNG SENSITIZATION-IMMEDIATE

Study-no.: T6039897

Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
1	00:00:15	10.8	9.27	2.60	115.0	284.2	.22	.36
2	00:00:30	11.0	9.58	2.82	100.9	258.4	.25	.40
3	00:00:45	11.3	9.85	3.05	92.5	255.1	.27	.40
4	00:01:00	11.5	9.58	2.89	92.0	259.5	.27	.40
5	00:01:15	11.8	10.15	2.95	89.3	258.9	.28	.41
6	00:01:30	12.0	7.80	2.95	82.2	237.8	.36	.44
7	00:01:45	12.3	8.88	2.98	83.7	243.9	.30	.44
8	00:02:00	12.5	9.70	3.14	81.7	240.7	.30	.46
9	00:02:15	12.8	10.15	3.20	84.1	255.7	.30	.41
10	00:02:30	13.0	9.48	3.16	85.1	257.3	.31	.43
11	00:02:45	13.3	10.68	3.19	86.4	265.6	.30	.41
12	00:03:00	13.5	8.70	3.16	86.6	262.6	.31	.44
13	00:03:15	13.8	9.10	3.05	85.4	259.1	.30	.42
14	00:03:30	14.0	9.63	3.23	84.8	254.5	.30	.43
15	00:03:45	14.3	9.98	3.36	82.0	254.6	.30	.46
16	00:04:00	14.5	9.13	3.12	83.0	259.4	.31	.44
17	00:04:15	14.8	8.80	3.08	82.2	251.6	.31	.43
18	00:04:30	15.0	9.40	3.24	80.9	252.5	.32	.44
19	00:04:45	15.3	9.48	3.33	81.5	254.6	.32	.44
20	00:05:00	15.5	9.27	3.24	79.0	250.0	.32	.46
21	00:05:15	15.8	9.65	3.34	77.7	247.8	.33	.45
22	00:05:30	16.0	9.35	3.40	77.3	249.2	.34	.45
23	00:05:45	16.3	9.48	3.32	78.5	250.0	.32	.45
24	00:06:00	16.5	9.23	3.32	78.3	251.0	.33	.46
25	00:06:15	16.8	10.33	3.47	77.8	255.4	.32	.45
26	00:06:30	17.0	10.08	3.40	75.5	249.7	.32	.48
27	00:06:45	17.3	9.70	3.30	79.8	259.4	.32	.44
28	00:07:00	17.5	9.38	3.38	77.8	252.3	.34	.47
29	00:07:15	17.8	9.45	3.37	77.7	247.1	.34	.46
30	00:07:30	18.0	9.00	3.36	75.8	243.9	.34	.47
31	00:07:45	18.3	9.60	3.29	76.9	246.1	.32	.45
32	00:08:00	18.5	9.40	3.30	78.6	248.7	.33	.45
33	00:08:15	18.8	9.03	3.26	76.7	238.5	.34	.47
34	00:08:30	19.0	9.18	3.36	75.9	237.6	.33	.46
35	00:08:45	19.3	10.67	3.42	77.8	248.8	.32	.45
36	00:09:00	19.5	9.65	3.46	76.9	238.2	.34	.48
37	00:09:15	19.8	9.68	3.46	75.5	236.0	.33	.51
38	00:09:30	20.0	9.50	3.48	74.5	243.4	.34	.50
39	00:09:45	20.3	9.35	3.34	74.7	239.0	.34	.49
40	00:10:00	20.5	9.05	3.38	73.3	236.2	.36	.50
41	00:10:15	20.8	9.58	3.42	74.0	236.3	.35	.49
42	00:10:30	21.0	9.05	3.49	73.3	234.3	.35	.51

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
43	00:10:45	21.3	9.48	3.35	74.1	236.4	.35	.48
44	00:11:00	21.5	9.45	3.41	74.0	238.1	.34	.48
45	00:11:15	21.8	9.70	3.47	73.4	238.1	.35	.50
46	00:11:30	22.0	9.58	3.42	71.7	235.0	.36	.50
47	00:11:45	22.3	9.13	3.43	70.3	227.0	.37	.51
48	00:12:00	22.5	9.45	3.46	71.4	229.1	.36	.51
49	00:12:15	22.8	9.15	3.36	67.4	219.7	.34	.56
50	00:12:30	23.0	9.65	3.49	71.7	233.5	.35	.49
51	00:12:45	23.3	9.63	3.19	76.0	237.2	.32	.46
52	00:13:00	23.5	9.83	3.45	74.9	232.6	.34	.51
53	00:13:15	23.8	9.95	3.56	72.5	233.7	.35	.50
54	00:13:30	24.0	10.08	3.46	73.1	239.0	.34	.49
55	00:13:45	24.3	9.55	3.42	72.4	236.3	.35	.51
56	00:14:00	24.5	9.35	3.38	72.2	231.1	.36	.50
57	00:14:15	24.8	9.55	3.38	71.9	232.2	.35	.50
58	00:14:30	25.0	9.65	3.41	67.6	217.8	.36	.60
59	00:14:45	25.3	9.00	3.38	70.4	225.6	.36	.52
60	00:15:00	25.5	10.30	3.21	70.7	222.4	.36	.56
61	00:15:15	25.8	8.90	3.36	70.5	222.4	.35	.50
62	00:15:30	26.0	9.70	3.44	71.7	229.3	.36	.51
63	00:15:45	26.3	9.05	3.24	72.3	227.1	.35	.51
64	00:16:00	26.5	9.05	3.39	70.5	223.8	.35	.53
65	00:16:15	26.8	9.58	3.41	69.7	225.3	.36	.53
66	00:16:30	27.0	8.75	3.17	69.1	217.9	.36	.55
67	00:16:45	27.3	9.45	3.23	71.0	222.8	.35	.51
68	00:17:00	27.5	8.83	3.24	68.4	216.2	.36	.60
69	00:17:15	27.8	9.00	3.30	66.7	213.7	.35	.53
70	00:17:30	28.0	8.63	3.14	69.7	217.3	.33	.52
71	00:17:45	28.3	8.55	3.16	70.2	214.5	.35	.52
72	00:18:00	28.5	9.02	3.08	72.3	217.8	.33	.51
73	00:18:15	28.8	8.90	3.19	71.1	213.5	.34	.57
74	00:18:30	29.0	9.05	3.05	71.5	211.0	.33	.50
75	00:18:45	29.3	8.80	3.14	72.8	214.8	.35	.51
76	00:19:00	29.5	9.15	3.17	72.6	218.9	.34	.50
77	00:19:15	29.8	8.90	3.31	69.5	214.7	.35	.60
78	00:19:30	30.0	9.18	3.33	68.4	218.3	.35	.52
79	00:19:45	30.3	9.42	3.13	76.8	224.7	.33	.50
80	00:20:00	30.5	9.40	3.30	73.7	221.2	.35	.50
81	00:20:15	30.8	9.15	3.17	72.7	217.8	.33	.50
82	00:20:30	31.0	9.75	3.37	75.0	225.6	.34	.51
83	00:20:45	31.3	9.13	3.30	74.3	224.6	.34	.52
84	00:21:00	31.5	9.13	3.45	72.6	226.4	.35	.51

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/mir.	MV ml/min.	IT sec	ET sec
85	00:21:15	31.8	9.63	3.43	71.1	225.4	.36	.54
86	00:21:30	32.0	9.18	3.36	70.4	222.1	.33	.55
87	00:21:45	32.3	9.40	3.40	70.9	227.1	.35	.52
88	00:22:00	32.5	9.33	3.31	70.9	222.5	.33	.55
89	00:22:15	32.8	9.00	3.41	69.9	221.7	.35	.52
90	00:22:30	33.0	9.40	3.24	70.9	218.1	.34	.51
91	00:22:45	33.3	8.78	3.35	70.9	221.5	.35	.51
92	00:23:00	33.5	9.15	3.43	71.0	226.8	.35	.51
93	00:23:15	33.8	9.00	3.36	70.9	227.6	.35	.51
94	00:23:30	34.0	9.65	3.36	69.9	222.8	.35	.56
95	00:23:45	34.3	10.38	3.08	66.8	207.9	.34	.61
96	00:24:00	34.5	11.00	3.24	71.5	219.0	.34	.50
97	00:24:15	34.8	8.50	3.19	70.1	214.7	.36	.53
98	00:24:30	35.0	8.75	3.25	69.6	217.1	.36	.52
99	00:24:45	35.3	9.08	3.25	70.3	219.8	.35	.51
100	00:25:00	35.5	9.48	3.15	72.1	222.2	.33	.48
101	00:25:15	35.8	8.83	3.22	71.3	212.5	.37	.54
102	00:25:30	36.0	9.15	3.28	68.3	209.4	.36	.57
103	00:25:45	36.3	9.30	3.20	71.0	213.5	.33	.48
104	00:26:00	36.5	9.38	3.35	72.7	222.6	.34	.50
105	00:26:15	36.8	8.98	3.28	71.4	219.8	.35	.52
106	00:26:30	37.0	9.38	3.41	71.2	221.9	.34	.52
107	00:26:45	37.3	9.13	3.33	72.2	221.2	.35	.52
108	00:27:00	37.5	9.05	3.26	67.0	207.0	.35	.54
109	00:27:15	37.8	8.60	3.25	70.5	219.0	.34	.51
110	00:27:30	38.0	8.83	3.37	70.3	222.3	.35	.52
111	00:27:45	38.3	9.10	3.25	72.0	224.5	.33	.51
112	00:28:00	38.5	8.98	3.23	72.8	216.8	.34	.51
113	00:28:15	38.8	9.40	3.32	70.3	215.7	.35	.52
114	00:28:30	39.0	8.78	3.18	70.2	217.1	.35	.53
115	00:28:45	39.3	9.08	3.32	68.5	212.3	.36	.56
116	00:29:00	39.5	8.75	3.25	64.5	202.8	.35	.59
117	00:29:15	39.8	8.88	3.33	68.9	213.6	.35	.54
118	00:29:30	40.0	9.35	3.14	71.4	210.5	.34	.49
119	00:29:45	40.3	8.85	3.28	71.9	210.6	.35	.53
120	00:30:00	40.5	11.58	3.42	65.9	202.4	.37	.60
1	00:00:15	40.8	7.15	2.43	100.0	227.1	.24	.43
2	00:00:30	41.0	6.78	2.55	94.4	225.1	.26	.47
3	00:00:45	41.3	5.98	2.59	83.2	198.3	.30	.52
4	00:01:00	41.5	6.20	2.74	78.4	197.3	.30	.53
5	00:01:15	41.8	7.10	2.95	79.2	208.1	.30	.49
6	00:01:30	42.0	6.58	2.91	78.4	211.3	.32	.51

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2a

	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
7	00:01:45	42.3	6.68	2.91	74.8	206.9	.32	.52
8	00:02:00	42.5	6.70	2.94	73.5	205.6	.33	.51
9	00:02:15	42.8	6.80	3.03	73.2	207.0	.33	.51
10	00:02:30	43.0	7.07	3.06	72.4	209.8	.33	.50
11	00:02:45	43.3	6.80	2.92	74.2	212.4	.31	.50
12	00:03:00	43.5	6.78	2.97	73.9	209.3	.31	.52
13	00:03:15	43.8	7.15	2.90	76.8	215.4	.30	.49
14	00:03:30	44.0	7.58	3.00	78.3	221.0	.30	.49
15	00:03:45	44.3	7.63	3.21	75.1	217.0	.32	.53
16	00:04:00	44.5	7.48	2.99	72.8	202.5	.30	.53
17	00:04:15	44.8	7.53	3.17	77.1	215.9	.32	.48
18	00:04:30	45.0	7.98	3.31	77.0	235.1	.32	.49
19	00:04:45	45.3	7.93	3.20	77.8	235.3	.32	.49
20	00:05:00	45.5	7.93	3.02	77.8	224.1	.32	.50
21	00:05:15	45.8	7.85	3.28	73.7	218.9	.34	.52
22	00:05:30	46.0	9.60	3.33	72.1	221.9	.33	.52
23	00:05:45	46.3	8.30	3.46	70.1	221.7	.35	.52
24	00:06:00	46.5	8.35	3.39	70.2	223.9	.35	.52
25	00:06:15	46.8	8.28	3.43	70.5	224.4	.34	.53
26	00:06:30	47.0	8.25	3.43	69.3	220.5	.36	.53
27	00:06:45	47.3	8.45	3.52	68.3	220.4	.35	.54
28	00:07:00	47.5	8.25	3.34	69.5	221.0	.35	.52
29	00:07:15	47.8	8.23	3.46	65.8	210.1	.36	.59
30	00:07:30	48.0	8.00	3.30	68.5	215.9	.34	.52
31	00:07:45	48.3	8.58	3.39	70.3	226.3	.34	.53
32	00:08:00	48.5	8.25	3.27	71.0	225.6	.33	.52
33	00:08:15	48.8	8.68	3.20	68.2	211.9	.35	.63
34	00:08:30	49.0	8.18	3.24	68.6	211.3	.35	.55
35	00:08:45	49.3	8.53	3.21	70.4	217.4	.34	.51
36	00:09:00	49.5	8.43	3.38	70.5	222.5	.35	.53
37	00:09:15	49.8	7.78	3.19	69.4	217.5	.34	.53
38	00:09:30	50.0	7.50	3.11	70.6	212.2	.34	.53
39	00:09:45	50.3	8.05	3.35	68.9	211.3	.35	.53
40	00:10:00	50.5	7.83	3.32	65.7	201.3	.37	.63
41	00:10:15	50.8	8.30	3.25	66.6	206.7	.35	.53
42	00:10:30	51.0	8.40	3.29	70.2	217.4	.34	.53
43	00:10:45	51.3	8.83	3.34	70.7	221.1	.34	.54
44	00:11:00	51.5	8.23	3.12	70.2	219.2	.33	.55
45	00:11:15	51.8	6.53	2.84	70.2	196.7	.36	.54
46	00:11:30	52.0	7.28	3.08	71.3	201.9	.33	.53
47	00:11:45	52.3	7.90	3.15	72.8	213.7	.33	.52
48	00:12:00	52.5	7.98	3.28	71.0	216.5	.34	.54

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
49	00:12:15	52.8	7.55	3.20	69.5	210.1	.35	.55
50	00:12:30	53.0	7.80	3.10	72.4	212.3	.32	.52
51	00:12:45	53.3	8.30	3.24	71.9	218.0	.33	.52
52	00:13:00	53.5	8.28	3.23	69.6	212.6	.33	.57
53	00:13:15	53.8	8.88	3.18	69.8	209.5	.33	.53
54	00:13:30	54.0	7.82	3.14	70.9	209.4	.33	.52
55	00:13:45	54.3	8.60	3.29	71.8	216.0	.34	.55
56	00:14:00	54.5	8.67	3.16	67.5	206.1	.32	.61
57	00:14:15	54.8	8.40	3.25	71.1	218.1	.33	.53
58	00:14:30	55.0	8.38	3.14	73.0	221.8	.32	.51
59	00:14:45	55.3	8.50	3.16	73.3	221.7	.32	.50
60	00:15:00	55.5	8.13	3.13	74.5	216.9	.33	.53
61	00:15:15	55.8	7.88	3.08	72.1	217.6	.32	.52
62	00:15:30	56.0	8.13	3.32	70.3	211.5	.36	.57
63	00:15:45	56.3	8.13	3.24	67.0	204.5	.35	.61
64	00:16:00	56.5	7.78	3.20	68.5	211.3	.34	.53
65	00:16:15	56.8	7.95	3.36	68.4	214.3	.35	.53
66	00:16:30	57.0	8.53	3.35	69.7	220.3	.34	.52
67	00:16:45	57.3	8.58	3.22	67.2	208.0	.34	.59
68	00:17:00	57.5	8.20	3.39	67.9	207.7	.34	.52
69	00:17:15	57.8	8.38	3.18	73.2	218.7	.32	.49
70	00:17:30	58.0	8.50	3.27	76.1	222.4	.34	.49
71	00:17:45	58.3	8.55	2.99	75.2	224.0	.32	.49
72	00:18:00	58.5	8.80	3.01	79.3	217.0	.31	.50
73	00:18:15	58.8	7.55	3.14	74.1	219.3	.34	.52
74	00:18:30	59.0	8.25	3.22	72.0	220.2	.35	.50
75	00:18:45	59.3	8.25	3.38	71.1	221.2	.36	.50
76	00:19:00	59.5	10.48	3.01	81.3	223.0	.30	.45
77	00:19:15	59.8	9.15	3.16	81.3	225.8	.33	.46
78	00:19:30	60.0	9.10	3.23	84.1	235.9	.33	.47
79	00:19:45	60.3	8.85	3.40	77.0	238.0	.34	.48
80	00:20:00	60.5	9.60	3.20	74.1	230.7	.34	.50
81	00:20:15	60.8	8.90	3.33	71.7	225.7	.34	.51
82	00:20:30	61.0	9.10	3.36	72.3	226.5	.34	.50
83	00:20:45	61.3	9.38	3.24	72.8	225.1	.33	.49
84	00:21:00	61.5	9.43	3.29	73.4	223.8	.33	.49
85	00:21:15	61.8	9.15	3.29	72.5	218.2	.34	.51
86	00:21:30	62.0	8.38	3.16	71.8	213.5	.33	.52
87	00:21:45	62.3	8.75	3.34	71.9	219.0	.34	.50
88	00:22:00	62.5	14.23	3.45	69.2	218.8	.35	.68
89	00:22:15	62.8	10.00	3.29	68.6	212.6	.33	.56
90	00:22:30	63.0	9.48	3.42	71.9	215.8	.34	.51

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
91	00:22:45	63.3	8.60	3.10	80.4	218.7	.31	.49
92	00:23:00	63.5	10.20	3.26	80.6	218.0	.32	.48
93	00:23:15	63.8	9.80	3.28	79.6	223.0	.32	.48
94	00:23:30	64.0	9.65	3.49	76.7	231.6	.32	.49
95	00:23:45	64.3	10.58	3.51	74.9	236.4	.33	.49
96	00:24:00	64.5	10.18	3.45	73.9	233.0	.34	.50
97	00:24:15	64.8	8.25	3.22	72.8	221.8	.33	.52
98	00:24:30	65.0	11.77	3.18	76.7	219.5	.30	.48
99	00:24:45	65.3	10.55	3.22	78.4	226.1	.31	.49
100	00:25:00	65.5	10.20	3.22	79.2	229.0	.30	.47
101	00:25:15	65.8	10.18	3.32	80.5	228.7	.32	.49
102	00:25:30	66.0	10.10	3.51	74.0	223.7	.42	.60
103	00:25:45	66.3	11.18	3.23	71.6	213.7	.36	.56
104	00:26:00	66.5	10.20	3.50	76.7	227.8	.33	.48
105	00:26:15	66.8	10.40	3.30	76.8	230.5	.31	.49
106	00:26:30	67.0	8.80	3.39	73.9	226.2	.34	.49
107	00:26:45	67.3	8.80	3.42	72.1	224.4	.35	.50
108	00:27:00	67.5	8.90	3.48	70.3	221.6	.35	.52
109	00:27:15	67.8	8.58	3.31	72.0	221.8	.34	.49
110	00:27:30	68.0	8.63	3.35	71.7	220.3	.35	.50
111	00:27:45	68.3	8.60	3.41	70.6	222.0	.35	.51
112	00:28:00	68.5	8.48	3.33	71.4	225.2	.34	.51
113	00:28:15	68.8	8.70	3.26	70.9	217.0	.34	.52
114	00:28:30	69.0	9.60	3.19	71.3	201.1	.33	.57
115	00:28:45	69.3	10.95	3.23	74.4	213.1	.31	.51
116	00:29:00	69.5	11.95	3.36	78.3	224.6	.32	.50
117	00:29:15	69.8	12.17	3.46	81.7	250.9	.31	.48
118	00:29:30	70.0	11.43	3.57	81.5	254.3	.32	.50
119	00:29:45	70.3	10.70	3.72	77.0	261.9	.35	.50
120	00:30:00	70.5	11.63	3.52	75.9	258.2	.33	.49

Control-Period: 0.0 - 10.5 (minutes)
Exposure-Period: 10.8 - 40.5 (minutes)
Recovery-Period: 40.8 - 70.5 (minutes)

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
1	00:00:15	.3	11.73	3.43	101.3	306.7	.24	.37
2	00:00:30	.5	12.48	3.60	100.7	321.1	.24	.36
3	00:00:45	.8	12.48	3.49	102.3	320.5	.25	.35
4	00:01:00	1.0	12.65	3.48	100.9	315.2	.24	.35
5	00:01:15	1.3	12.65	3.70	100.1	318.0	.25	.37
6	00:01:30	1.5	13.60	3.81	98.1	319.1	.25	.36
7	00:01:45	1.8	12.93	3.81	95.8	312.9	.27	.37
8	00:02:00	2.0	13.65	4.00	94.5	311.5	.27	.37
9	00:02:15	2.3	13.60	3.91	96.3	316.9	.25	.35
10	00:02:30	2.5	13.70	3.71	98.5	319.4	.26	.35
11	00:02:45	2.8	13.00	3.66	96.9	300.3	.26	.36
12	00:03:00	3.0	13.60	3.73	97.5	305.6	.25	.35
13	00:03:15	3.3	13.58	3.71	97.5	309.0	.25	.36
14	00:03:30	3.5	13.73	3.94	98.6	311.7	.26	.36
15	00:03:45	3.8	13.38	3.77	98.9	313.1	.25	.36
16	00:04:00	4.0	12.58	3.82	97.4	310.7	.25	.37
17	00:04:15	4.3	12.83	3.83	96.4	315.7	.26	.37
18	00:04:30	4.5	13.40	3.98	95.6	310.6	.27	.37
19	00:04:45	4.8	14.00	3.99	96.0	313.1	.26	.36
20	00:05:00	5.0	14.48	4.17	95.1	320.2	.27	.37
21	00:05:15	5.3	14.63	4.09	95.0	320.4	.25	.36
22	00:05:30	5.5	14.56	3.85	98.4	328.1	.25	.35
23	00:05:45	5.8	13.42	3.69	99.0	319.4	.26	.36
24	00:06:00	6.0	12.23	3.78	96.6	320.9	.27	.37
25	00:06:15	6.3	12.83	4.02	94.4	316.2	.27	.37
26	00:06:30	6.5	13.43	4.09	93.1	313.9	.31	.36
27	00:06:45	6.8	14.10	3.85	96.3	319.9	.27	.34
28	00:07:00	7.0	13.60	3.98	97.1	320.7	.27	.35
29	00:07:15	7.3	14.18	4.02	97.1	323.3	.25	.36
30	00:07:30	7.5	14.75	3.84	99.8	326.4	.24	.35
31	00:07:45	7.8	10.05	2.84	100.1	305.9	.24	.39
32	00:08:00	8.0	8.40	2.93	92.0	256.7	.26	.42
33	00:08:15	8.3	8.75	2.94	90.0	259.4	.26	.42
34	00:08:30	8.5	9.78	3.20	88.9	267.0	.28	.40
35	00:08:45	8.8	10.33	3.23	89.5	273.5	.27	.40
36	00:09:00	9.0	8.58	2.49	89.7	245.2	.26	.42
37	00:09:15	9.3	10.92	2.68	92.8	230.5	.26	.39
38	00:09:30	9.5	8.85	3.14	87.8	234.3	.30	.41
39	00:09:45	9.8	10.30	3.47	85.9	253.5	.30	.40
40	00:10:00	10.0	9.88	3.27	85.4	258.4	.30	.40
1	00:00:15	10.3	10.38	2.95	106.7	296.8	.23	.36
2	00:00:30	10.5	10.23	3.00	99.6	285.9	.25	.37

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
3	00:00:45	10.8	10.15	3.10	94.5	275.1	.26	.39
4	00:01:00	11.0	10.00	3.04	92.0	273.0	.28	.39
5	00:01:15	11.3	10.60	3.13	91.5	278.0	.28	.38
6	00:01:30	11.5	10.00	3.07	90.9	274.6	.27	.39
7	00:01:45	11.8	10.60	3.28	89.0	275.3	.28	.39
8	00:02:00	12.0	10.25	3.33	86.9	271.5	.29	.41
9	00:02:15	12.3	10.20	3.29	86.0	270.1	.29	.41
10	00:02:30	12.5	10.92	3.45	85.7	273.1	.30	.40
11	00:02:45	12.8	10.55	3.34	86.3	278.4	.29	.40
12	00:03:00	13.0	10.05	3.36	85.4	272.7	.29	.41
13	00:03:15	13.3	10.10	3.35	83.7	264.3	.30	.42
14	00:03:30	13.5	9.90	3.27	84.7	265.9	.29	.41
15	00:03:45	13.8	10.68	3.51	85.4	275.3	.29	.40
16	00:04:00	14.0	10.90	3.51	86.1	281.5	.29	.40
17	00:04:15	14.3	10.63	3.36	86.2	282.8	.28	.41
18	00:04:30	14.5	10.65	3.47	85.2	274.7	.29	.41
19	00:04:45	14.8	10.80	3.42	86.4	277.9	.28	.40
20	00:05:00	15.0	11.00	3.61	85.4	277.0	.29	.42
21	00:05:15	15.3	10.48	3.43	85.1	275.5	.29	.42
22	00:05:30	15.5	10.95	3.44	84.5	272.1	.29	.41
23	00:05:45	15.8	11.05	3.50	85.4	271.2	.29	.41
24	00:06:00	16.0	10.65	3.39	84.7	276.4	.29	.42
25	00:06:15	16.3	10.75	3.43	85.1	271.6	.29	.41
26	00:06:30	16.5	11.10	3.53	85.2	275.1	.30	.42
27	00:06:45	16.8	10.83	3.51	83.6	269.7	.30	.43
28	00:07:00	17.0	10.68	3.42	83.5	268.7	.30	.43
29	00:07:15	17.3	10.80	3.53	82.9	272.6	.30	.42
30	00:07:30	17.5	10.77	3.47	82.6	275.5	.29	.43
31	00:07:45	17.8	11.08	3.43	84.2	276.3	.28	.41
32	00:08:00	18.0	11.08	3.30	87.4	281.3	.27	.41
33	00:08:15	18.3	10.55	3.59	85.8	275.1	.30	.43
34	00:08:30	18.5	10.90	3.54	83.3	274.3	.30	.43
35	00:08:45	18.8	10.73	3.49	83.5	276.7	.29	.42
36	00:09:00	19.0	11.05	3.44	85.7	279.3	.28	.41
37	00:09:15	19.3	10.38	3.44	86.1	279.8	.30	.43
38	00:09:30	19.5	10.77	3.50	83.2	276.6	.30	.43
39	00:09:45	19.8	10.53	3.45	82.7	273.8	.30	.42
40	00:10:00	20.0	10.05	3.26	83.3	270.4	.30	.42
41	00:10:15	20.3	10.33	3.44	83.1	270.0	.30	.42
42	00:10:30	20.5	10.40	3.39	82.0	266.9	.30	.43
43	00:10:45	20.8	10.38	3.57	81.7	270.0	.31	.43
44	00:11:00	21.0	10.85	3.43	82.3	272.3	.30	.43

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
45	00:11:15	21.3	10.63	3.53	82.6	278.2	.30	.43
46	00:11:30	21.5	10.50	3.45	83.9	282.4	.29	.41
47	00:11:45	21.8	10.58	3.59	82.2	274.2	.30	.44
48	00:12:00	22.0	10.85	3.28	87.3	278.9	.27	.40
49	00:12:15	22.3	10.18	3.46	85.8	274.1	.30	.43
50	00:12:30	22.5	11.02	3.68	82.5	276.9	.30	.43
51	00:12:45	22.8	11.05	3.38	83.3	273.9	.29	.41
52	00:13:00	23.0	10.33	3.41	85.6	278.2	.30	.42
53	00:13:15	23.3	10.77	3.51	83.1	278.9	.30	.43
54	00:13:30	23.5	11.05	3.55	82.6	280.6	.30	.42
55	00:13:45	23.8	11.48	3.48	85.0	287.7	.29	.40
56	00:14:00	24.0	10.75	3.64	83.9	287.3	.30	.42
57	00:14:15	24.3	11.90	3.83	82.8	287.8	.30	.42
58	00:14:30	24.5	10.93	3.58	83.2	282.3	.29	.42
59	00:14:45	24.8	10.73	3.58	83.7	288.3	.30	.42
60	00:15:00	25.0	11.00	3.61	83.4	288.3	.30	.42
61	00:15:15	25.3	11.20	3.51	84.5	287.7	.30	.40
62	00:15:30	25.5	10.45	3.47	84.0	278.5	.30	.43
63	00:15:45	25.8	10.80	3.43	84.0	277.7	.29	.42
64	00:16:00	26.0	10.68	3.51	84.1	279.3	.30	.42
65	00:16:15	26.3	11.70	3.55	84.4	284.1	.29	.41
66	00:16:30	26.5	11.15	3.59	86.0	280.6	.30	.42
67	00:16:45	26.8	11.67	3.57	84.7	282.0	.30	.42
68	00:17:00	27.0	11.43	3.62	85.1	287.8	.30	.41
69	00:17:15	27.3	11.70	3.76	83.1	285.7	.31	.43
70	00:17:30	27.5	10.95	3.49	82.8	281.0	.30	.43
71	00:17:45	27.8	11.30	3.60	83.6	279.5	.30	.42
72	00:18:00	28.0	11.13	3.73	81.6	279.2	.31	.44
73	00:18:15	28.3	11.35	3.72	81.2	282.2	.30	.43
74	00:18:30	28.5	11.68	3.61	83.4	284.1	.30	.42
75	00:18:45	28.8	11.28	3.69	82.3	281.0	.31	.42
76	00:19:00	29.0	11.03	3.54	82.9	283.9	.31	.42
77	00:19:15	29.3	11.50	3.47	84.7	286.2	.28	.39
78	00:19:30	29.5	12.00	3.49	92.0	292.9	.27	.39
79	00:19:45	29.8	11.65	3.84	85.8	291.7	.30	.42
80	00:20:00	30.0	11.75	3.59	85.9	289.4	.29	.41
81	00:20:15	30.3	11.48	3.75	84.3	290.4	.30	.43
82	00:20:30	30.5	11.20	3.59	83.4	289.2	.29	.42
83	00:20:45	30.8	12.65	3.48	85.8	290.8	.27	.40
84	00:21:00	31.0	10.50	3.52	88.6	286.8	.30	.42
85	00:21:15	31.3	11.23	3.58	84.7	289.3	.31	.41
86	00:21:30	31.5	11.28	3.59	83.4	289.6	.31	.42

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
87	00:21:45	31.8	10.98	3.60	81.8	281.8	.30	.43
88	00:22:00	32.0	9.95	3.41	81.6	272.8	.31	.44
89	00:22:15	32.3	10.43	3.54	80.1	269.4	.31	.44
90	00:22:30	32.5	10.58	3.66	78.7	261.9	.32	.46
91	00:22:45	32.8	9.93	3.42	78.5	260.3	.31	.44
92	00:23:00	33.0	10.60	3.45	81.4	266.8	.31	.44
93	00:23:15	33.3	10.00	3.59	78.9	267.7	.32	.45
94	00:23:30	33.5	10.40	3.60	79.2	274.0	.31	.44
95	00:23:45	33.8	10.48	3.60	80.1	276.1	.30	.44
96	00:24:00	34.0	10.95	3.56	81.1	279.0	.30	.43
97	00:24:15	34.3	11.45	3.44	83.1	271.0	.30	.43
98	00:24:30	34.5	10.53	3.57	81.9	272.5	.31	.43
99	00:24:45	34.8	10.93	3.66	82.2	276.8	.31	.42
100	00:25:00	35.0	10.93	3.43	84.0	274.6	.29	.41
101	00:25:15	35.3	10.63	3.62	82.2	272.9	.31	.45
102	00:25:30	35.5	11.55	3.67	81.7	280.8	.30	.43
103	00:25:45	35.8	10.95	3.64	85.1	282.7	.31	.43
104	00:26:00	36.0	11.30	3.75	82.6	283.4	.30	.43
105	00:26:15	36.3	11.60	3.51	89.1	284.8	.29	.40
106	00:26:30	36.5	10.68	3.56	84.7	283.8	.31	.42
107	00:26:45	36.8	11.63	3.61	87.2	285.0	.30	.41
108	00:27:00	37.0	10.75	3.60	84.9	281.2	.31	.44
109	00:27:15	37.3	10.58	3.62	80.8	270.1	.32	.44
110	00:27:30	37.5	10.68	3.67	79.3	273.2	.32	.45
111	00:27:45	37.8	11.18	3.82	78.6	273.9	.32	.45
112	00:28:00	38.0	11.10	3.58	81.9	274.0	.31	.44
113	00:28:15	38.3	9.83	3.36	80.3	267.4	.31	.44
114	00:28:30	38.5	11.05	3.73	78.8	265.9	.31	.46
115	00:28:45	38.8	10.95	3.77	78.8	266.4	.32	.46
116	00:29:00	39.0	10.28	3.67	77.9	261.7	.31	.45
117	00:29:15	39.3	10.80	3.60	79.6	272.6	.30	.44
118	00:29:30	39.5	10.33	3.39	84.0	269.4	.29	.43
119	00:29:45	39.8	9.85	3.54	80.4	266.2	.32	.46
120	00:30:00	40.0	9.88	3.63	77.6	259.7	.33	.47
1	00:00:15	40.3	5.83	2.16	89.6	183.3	.30	.44
2	00:00:30	40.5	5.95	2.51	79.9	181.4	.33	.48
3	00:00:45	40.8	5.95	2.59	74.2	182.1	.36	.48
4	00:01:00	41.0	6.48	2.87	71.8	193.3	.36	.50
5	00:01:15	41.3	6.85	2.93	72.3	203.0	.35	.48
6	00:01:30	41.5	6.70	2.88	72.3	204.6	.35	.48
7	00:01:45	41.8	7.65	2.87	75.9	217.7	.32	.46
8	00:02:00	42.0	7.43	2.92	76.8	219.6	.32	.47

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
9	00:02:15	42.3	7.75	3.12	75.4	220.1	.33	.48
10	00:02:30	42.5	7.65	3.24	74.4	223.1	.34	.48
11	00:02:45	42.8	7.80	3.10	75.1	221.5	.32	.48
12	00:03:00	43.0	7.75	3.05	76.1	227.0	.32	.47
13	00:03:15	43.3	8.03	3.10	77.7	235.5	.31	.46
14	00:03:30	43.5	8.13	3.00	80.2	243.5	.30	.44
15	00:03:45	43.8	8.20	3.12	79.3	236.8	.31	.45
16	00:04:00	44.0	8.53	3.09	80.4	238.1	.31	.45
17	00:04:15	44.3	8.15	2.91	80.7	234.6	.31	.46
18	00:04:30	44.5	8.77	3.12	80.2	236.3	.30	.44
19	00:04:45	44.8	8.68	3.03	85.4	246.1	.29	.43
20	00:05:00	45.0	8.65	3.08	83.3	247.3	.31	.44
21	00:05:15	45.3	9.00	3.10	83.1	247.8	.30	.43
22	00:05:30	45.5	8.95	3.14	82.8	246.3	.31	.44
23	00:05:45	45.8	9.00	3.53	78.1	239.5	.32	.50
24	00:06:00	46.0	8.50	2.72	81.6	240.5	.29	.42
25	00:06:15	46.3	8.65	2.78	90.3	230.9	.26	.42
26	00:06:30	46.5	10.85	2.98	92.2	246.4	.27	.41
27	00:06:45	46.8	8.80	2.67	93.1	241.8	.30	.42
28	00:07:00	47.0	10.00	2.83	91.0	241.3	.28	.40
29	00:07:15	47.3	8.58	2.80	90.3	233.1	.29	.44
30	00:07:30	47.5	9.85	2.89	92.3	242.9	.28	.41
31	00:07:45	47.8	12.02	2.94	96.1	255.6	.26	.39
32	00:08:00	48.0	7.55	2.90	87.9	232.3	.33	.45
33	00:08:15	48.3	12.40	2.75	90.6	233.3	.29	.38
34	00:08:30	48.5	7.60	3.21	84.2	230.4	.32	.48
35	00:08:45	48.8	8.10	3.27	76.7	234.3	.33	.49
36	00:09:00	49.0	8.83	3.40	76.2	243.3	.32	.48
37	00:09:15	49.3	8.88	3.19	77.5	247.0	.31	.45
38	00:09:30	49.5	8.73	3.22	78.9	248.0	.31	.44
39	00:09:45	49.8	8.15	3.09	80.0	239.7	.30	.46
40	00:10:00	50.0	8.48	3.13	79.7	235.3	.31	.46
41	00:10:15	50.3	8.55	3.17	79.9	240.6	.31	.44
42	00:10:30	50.5	7.80	2.77	78.8	238.3	.32	.47
43	00:10:45	50.8	6.03	2.04	73.8	184.5	.63	.45
44	00:11:00	51.0	6.00	2.20	76.3	168.6	.51	.44
45	00:11:15	51.3	7.00	2.85	77.4	192.5	.32	.48
46	00:11:30	51.5	7.50	2.91	75.7	206.5	.34	.48
47	00:11:45	51.8	7.83	2.99	75.1	214.8	.33	.48
48	00:12:00	52.0	7.50	2.83	75.9	206.1	.33	.46
49	00:12:15	52.3	8.23	2.98	78.5	222.0	.31	.45
50	00:12:30	52.5	8.40	3.12	78.5	230.2	.32	.46

LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

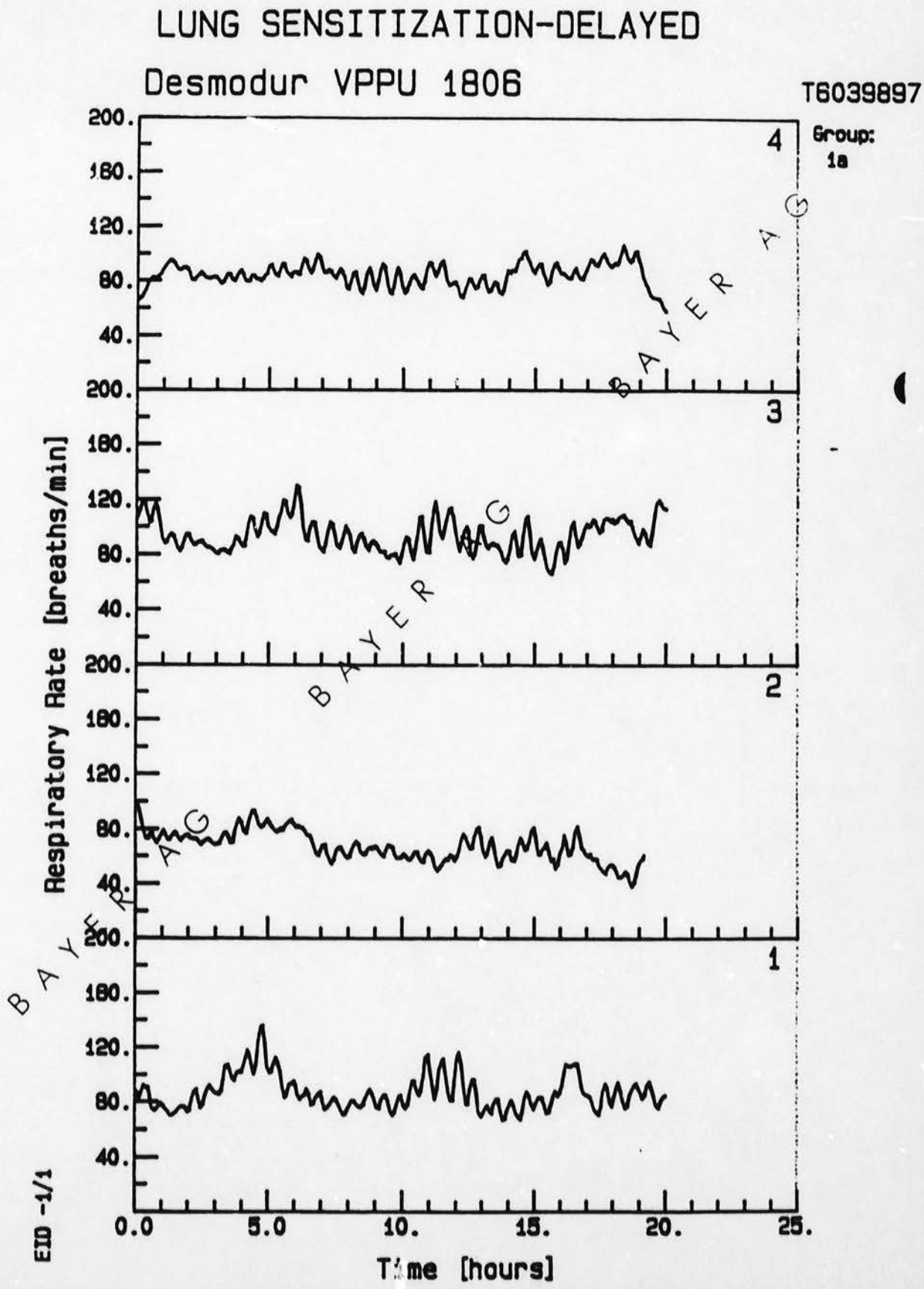
No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
51	00:12:45	52.8	8.30	3.09	77.4	230.4	.33	.45
52	00:13:00	53.0	9.42	3.07	78.3	230.1	.32	.45
53	00:13:15	53.3	7.78	3.05	76.9	221.3	.33	.47
54	00:13:30	53.5	7.98	3.00	76.3	222.9	.32	.46
55	00:13:45	53.8	8.43	2.94	77.8	228.9	.32	.47
56	00:14:00	54.0	8.73	3.35	76.0	225.2	.34	.48
57	00:14:15	54.3	9.23	3.01	77.2	234.6	.31	.45
58	00:14:30	54.5	8.20	3.19	78.1	224.4	.34	.48
59	00:14:45	54.8	8.00	3.08	76.3	228.8	.32	.47
60	00:15:00	55.0	7.75	3.11	74.2	222.7	.33	.50
61	00:15:15	55.3	8.05	3.05	75.1	220.7	.32	.47
62	00:15:30	55.5	8.98	3.24	76.0	232.6	.33	.47
63	00:15:45	55.8	9.00	3.29	75.8	239.3	.33	.47
64	00:16:00	56.0	8.75	3.11	76.1	235.9	.32	.47
65	00:16:15	56.3	9.10	3.28	76.1	226.5	.32	.47
66	00:16:30	56.5	9.02	3.36	76.1	235.9	.33	.47
67	00:16:45	56.8	8.70	3.07	77.8	241.1	.31	.46
68	00:17:00	57.0	9.05	3.25	78.0	241.8	.31	.45
69	00:17:15	57.3	9.78	2.89	81.8	240.3	.30	.43
70	00:17:30	57.5	7.88	3.01	80.1	222.5	.31	.47
71	00:17:45	57.8	8.23	3.04	77.6	227.5	.32	.47
72	00:18:00	58.0	8.85	3.09	78.0	233.3	.31	.46
73	00:18:15	58.3	8.43	3.08	76.7	228.0	.32	.48
74	00:18:30	58.5	8.48	3.14	76.0	229.5	.32	.46
75	00:18:45	58.8	8.75	3.27	76.6	232.0	.32	.47
76	00:19:00	59.0	8.83	3.00	76.9	231.5	.31	.49
77	00:19:15	59.3	7.80	2.87	77.2	225.4	.31	.47
78	00:19:30	59.5	8.65	3.04	80.2	232.3	.30	.44
79	00:19:45	59.8	9.13	3.20	80.3	242.9	.31	.46
80	00:20:00	60.0	9.50	3.29	79.3	242.7	.31	.46
81	00:20:15	60.3	9.25	3.37	78.3	241.6	.32	.46
82	00:20:30	60.5	9.20	3.22	78.9	248.5	.31	.44
83	00:20:45	60.8	9.68	3.38	78.5	252.3	.32	.45
84	00:21:00	61.0	7.83	2.82	80.7	245.2	.31	.43
85	00:21:15	61.3	8.50	3.16	78.3	234.1	.32	.47
86	00:21:30	61.5	8.88	3.14	77.7	233.8	.32	.45
87	00:21:45	61.8	8.58	3.10	78.2	238.5	.31	.45
88	00:22:00	62.0	8.88	3.12	78.2	238.2	.31	.46
89	00:22:15	62.3	8.45	3.11	78.4	239.5	.31	.46
90	00:22:30	62.5	8.50	3.15	79.9	235.1	.30	.45
91	00:22:45	62.8	9.20	3.25	79.9	245.8	.31	.46
92	00:23:00	63.0	8.90	3.17	78.1	241.0	.31	.48

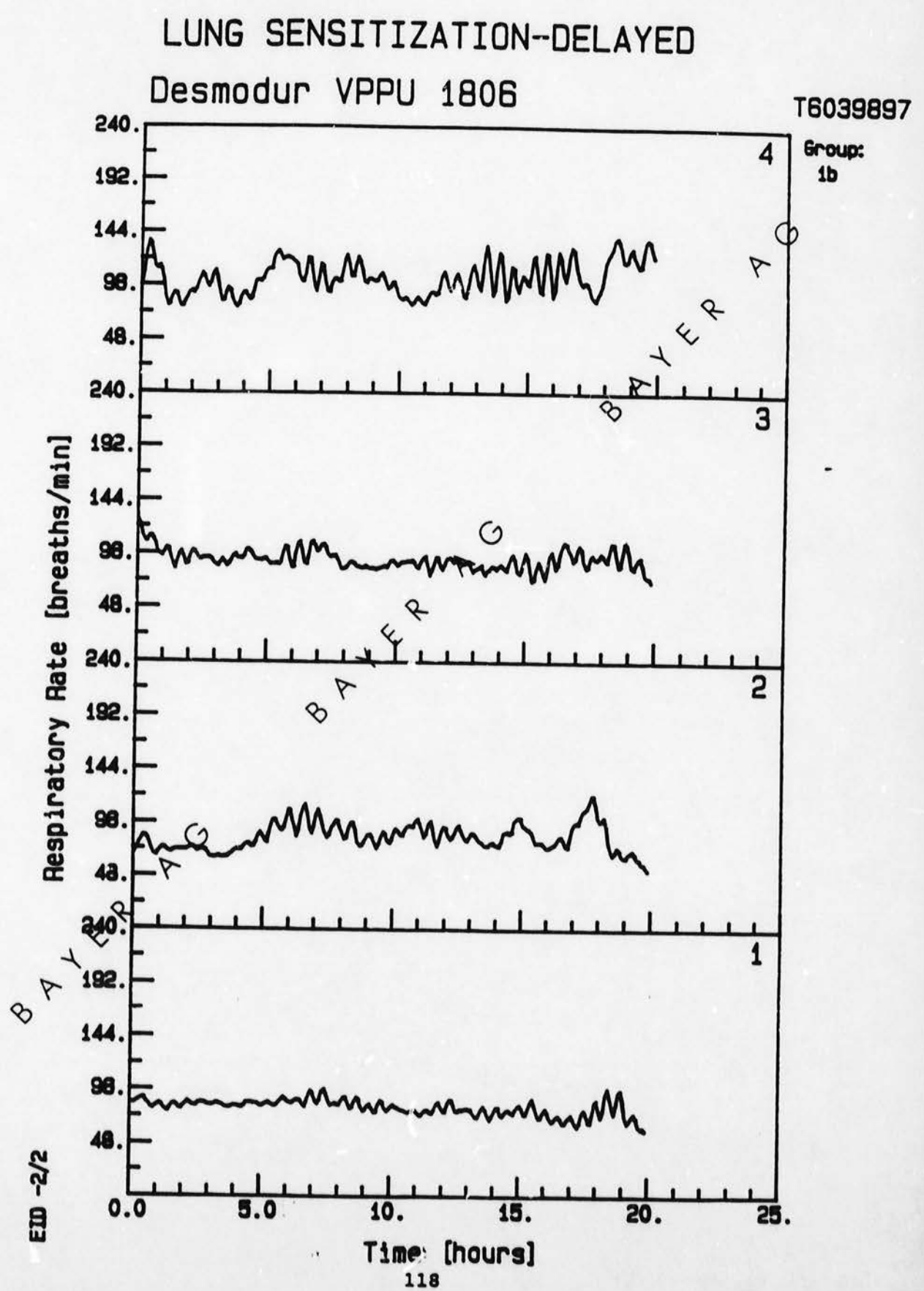
LUNG SENSITIZATION-IMMEDIATE
Study-no.: T6039897
Substance: Desmodur VPPU 1806

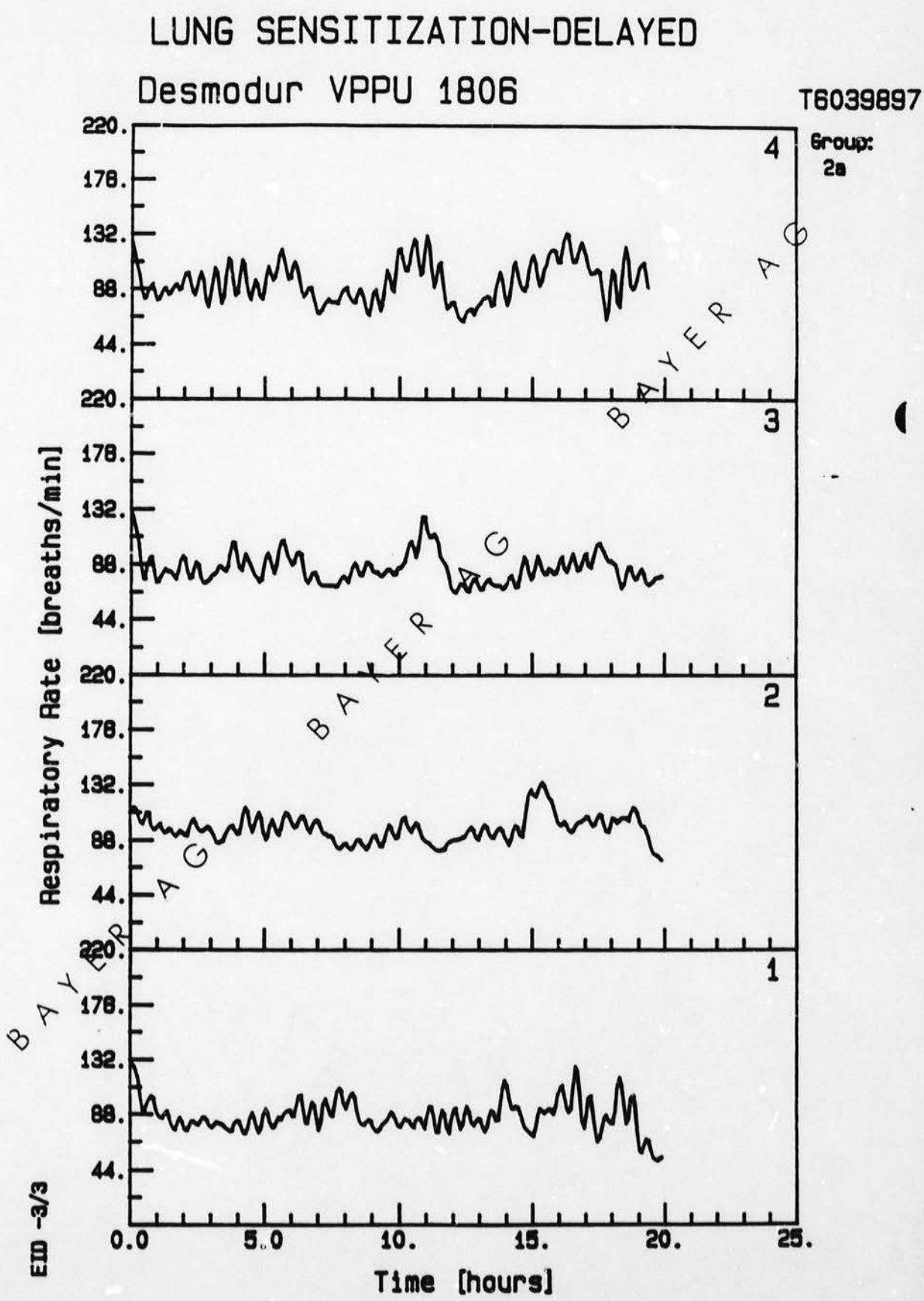
Group: 2b

No.	Time hh:mm:ss	Time min.	PEF ml/sec	TV ml	RATE b/min.	MV ml/min.	IT sec	ET sec
93	00:23:15	63.3	8.93	3.23	77.5	237.5	.31	.46
94	00:23:30	63.5	8.03	2.99	78.2	231.6	.31	.46
95	00:23:45	63.8	9.23	3.32	77.5	238.8	.33	.46
96	00:24:00	64.0	8.95	3.26	76.8	242.0	.33	.46
97	00:24:15	64.3	8.58	3.18	76.9	234.5	.33	.47
98	00:24:30	64.5	8.77	3.19	76.1	229.5	.33	.47
99	00:24:45	64.8	8.83	3.32	75.4	234.1	.34	.47
100	00:25:00	65.0	8.93	3.45	73.5	234.1	.35	.49
101	00:25:15	65.3	8.58	3.29	73.7	234.8	.32	.48
102	00:25:30	65.5	9.15	3.40	78.2	248.2	.32	.46
103	00:25:45	65.8	9.23	3.40	78.0	251.3	.32	.47
104	00:26:00	66.0	9.15	3.40	76.6	247.6	.33	.48
105	00:26:15	66.3	8.55	3.10	78.3	236.0	.32	.46
106	00:26:30	66.5	8.88	3.27	76.5	232.0	.33	.48
107	00:26:45	66.8	9.23	3.33	75.5	234.0	.32	.47
108	00:27:00	67.0	8.83	3.19	74.7	232.7	.33	.48
109	00:27:15	67.3	8.77	3.25	74.9	235.0	.32	.48
110	00:27:30	67.5	9.05	3.31	76.0	239.9	.31	.47
111	00:27:45	67.8	9.23	3.14	79.8	245.8	.30	.44
112	00:28:00	68.0	8.93	3.14	79.1	241.4	.32	.47
113	00:28:15	68.3	9.10	3.20	78.4	240.6	.31	.46
114	00:28:30	68.5	8.88	3.31	77.2	240.1	.32	.48
115	00:28:45	68.8	8.85	3.26	76.6	241.0	.32	.47
116	00:29:00	69.0	8.60	3.27	75.6	235.2	.32	.48
117	00:29:15	69.3	8.50	3.06	78.2	235.5	.30	.47
118	00:29:30	69.5	8.50	2.78	82.1	230.2	.29	.43
119	00:29:45	69.8	7.98	3.12	79.4	225.0	.32	.47
120	00:30:00	70.0	8.88	3.10	79.9	236.5	.30	.45

Control-Period: 0.0 - 10.0 (minutes)
Exposure-Period: 10.3 - 40.0 (minutes)
Recovery-Period: 40.3 - 70.0 (minutes)


LUNG SENSITIZATION-DELAYED
Desmodur VPPU 1806
T6039897
Group:
1a
4
3
2
1
Respiratory Rate [breaths/min]
200.
180.
120.
80.
40.
0.0
5.0
10.
15.
20.
25.
Time [hours]
EM -1/1
BAYER AG

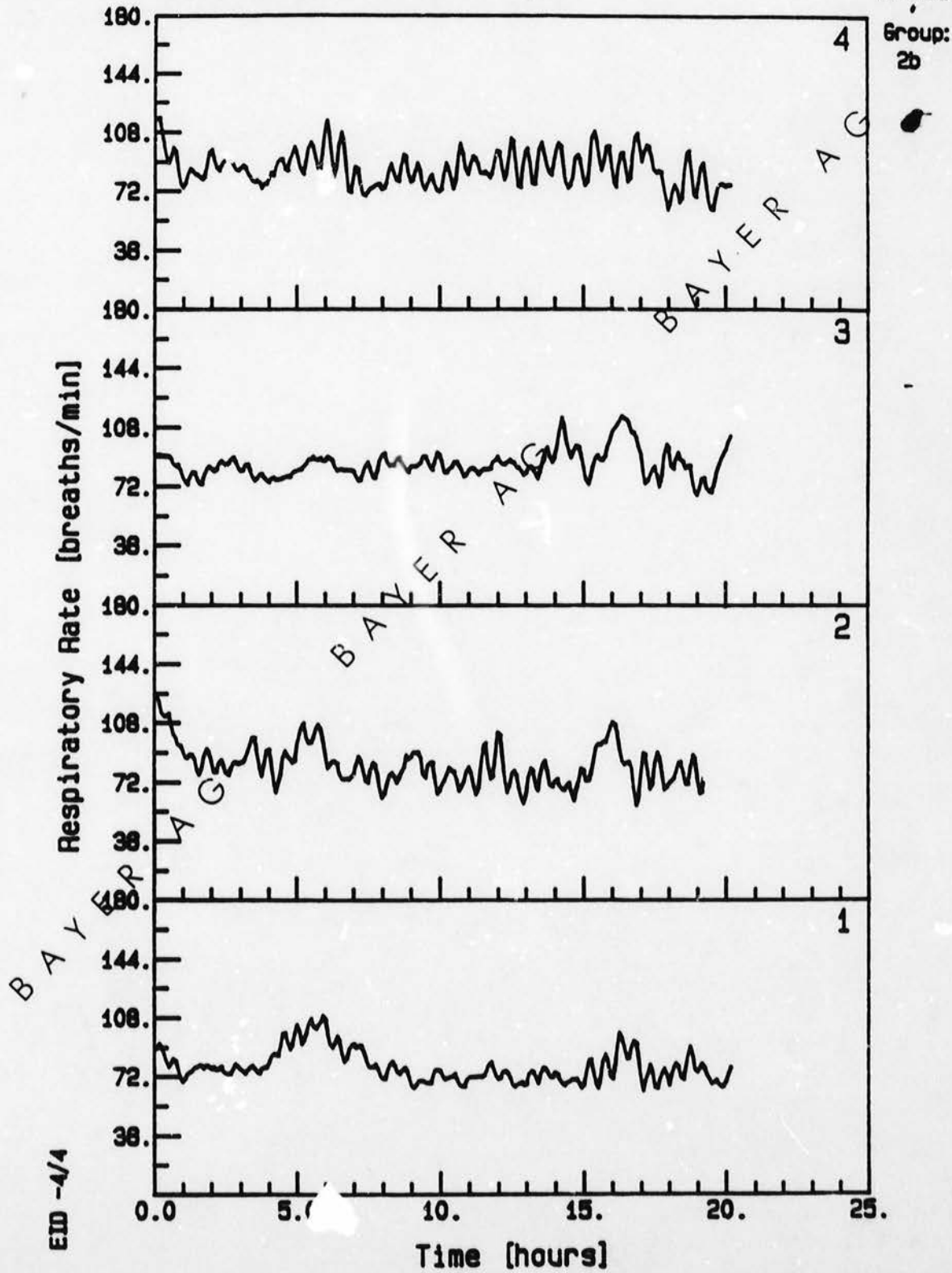

LUNG SENSITIZATION-DELAYED
Desmodur VPPU 1806
T6039897
Group:
1b
4
3
2
1
240.
192.
144.
96.
48.
Respiratory Rate [breaths/min]
BAYER AG
EM -2/2
0.0
5.0
10.
15.
20.
25.
Time [hours]


LUNG SENSITIZATION-DELAYED
Desmodur VPPU 1806
T6039897
Group:
2a
4
3
2
1
220.
178.
132.
88.
44.
Respiratory Rate [breaths/min]
0.0
5.0
10.
15.
20.
25.
Time [hours]
EM -3/3
BAYER AG

LUNG SENSITIZATION-DELAYED

Desmodur VPPU 1806

T6039897



LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

SUMMARY TABLE

(Data relative to control-period in %)

Group:	Min./ Max.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
1a	min.	60	33	75	101	72
	max.	122	132	148	164	119
1b	min.	66	57	53	71	73
	max.	111	128	92	136	98
2a	min.	40	78	46	44	57
	max.	99	131	93	96	94
2b	min.	76	42	73	48	63
	max.	141	142	132	93	98

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
3	00:03:00	3	111	115	88	65	95
8	00:08:00	8	91	84	88	74	85
13	00:13:00	13	151	94	90	83	105
18	00:18:00	18	81	77	96	74	82
23	00:23:00	23	65	74	143	68	87
28	00:28:00	28	62	68	136	69	84
33	00:33:00	33	87	86	146	71	97
38	00:38:00	38	118	53	131	79	95
43	00:43:00	43	86	62	99	86	83
48	00:48:00	48	65	94	89	81	82
53	00:53:00	53	96	88	118	76	94
58	00:58:00	58	72	71	136	78	89
63	01:03:00	63	67	60	108	78	78
68	01:08:00	68	70	65	77	78	73
73	01:13:00	73	75	89	82	82	82
78	01:18:00	78	79	87	83	99	87
83	01:23:00	83	77	62	89	112	85
88	01:28:00	88	74	73	85	109	85
93	01:33:00	93	70	64	96	113	86
98	01:38:00	98	69	88	108	110	94
103	01:43:00	103	71	82	96	81	83
108	01:48:00	108	76	74	75	82	76
113	01:53:00	113	74	63	72	78	72
118	01:58:00	118	75	72	72	74	73
123	02:03:00	123	72	76	78	79	76
128	02:08:00	128	67	75	105	92	85
133	02:13:00	133	78	84	111	80	87
138	02:18:00	138	77	74	95	86	83
143	02:23:00	143	62	73	94	83	78
148	02:28:00	148	110	74	101	78	91
153	02:33:00	153	121	78	94	97	97
158	02:38:00	158	75	62	83	94	79
163	02:43:00	163	73	59	78	81	73
168	02:48:00	168	74	64	78	83	75
173	02:53:00	173	94	74	85	82	84
178	02:58:00	178	104	84	71	87	87
183	03:03:00	183	84	69	97	78	82
188	03:08:00	188	65	70	85	77	74
193	03:13:00	193	70	64	85	82	75
198	03:18:00	198	69	73	79	75	74
203	03:23:00	203	71	73	88	74	76
208	03:28:00	208	77	63	72	73	71

LUNG SENSITIZATION-DELAYED
Study-no.: T6039857
Substance: D smodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
213	03:33:00	213	110	67	81	73	83
218	03:38:00	218	136	94	68	97	99
223	03:43:00	223	171	72	80	87	102
228	03:48:00	228	152	60	74	94	95
233	03:53:00	233	71	69	108	69	79
238	03:58:00	238	80	75	111	86	88
243	04:03:00	243	79	105	80	108	93
248	04:08:00	248	67	102	99	91	90
253	04:13:00	253	69	74	71	78	73
258	04:18:00	258	70	68	72	73	71
263	04:23:00	263	128	64	71	80	86
268	04:28:00	268	154	74	118	70	104
273	04:33:00	273	144	87	137	83	113
278	04:38:00	278	117	114	78	80	97
283	04:43:00	283	71	99	122	82	94
288	04:48:00	288	111	108	118	65	101
293	04:53:00	293	144	100	80	91	104
298	04:58:00	298	168	85	108	85	112
303	05:03:00	303	133	59	145	75	103
308	05:08:00	308	134	87	118	97	109
313	05:13:00	313	125	80	76	102	96
318	05:18:00	318	64	76	79	76	74
323	05:23:00	323	72	74	68	121	83
328	05:28:00	328	142	71	75	68	89
333	05:33:00	333	83	87	83	70	81
338	05:38:00	338	110	80	81	86	89
343	05:43:00	343	123	61	132	119	109
348	05:48:00	348	98	87	150	89	106
353	05:53:00	353	66	88	140	91	96
358	05:58:00	358	68	81	135	77	90
363	06:03:00	363	69	96	92	75	83
368	06:08:00	368	116	95	119	77	102
373	06:13:00	373	106	96	143	76	105
378	06:18:00	378	67	81	145	83	94
383	06:23:00	383	112	73	145	68	100
388	06:28:00	388	118	90	120	103	108
393	06:33:00	393	65	91	71	111	85
398	06:38:00	398	67	72	63	123	81
403	06:43:00	403	100	77	67	81	81
408	06:48:00	408	64	71	90	67	73
413	06:53:00	413	68	72	90	85	79
418	06:58:00	418	62	64	149	113	97

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
423	07:03:00	423	80	46	87	103	79
428	07:08:00	428	120	42	97	108	91
433	07:13:00	433	117	66	72	93	87
438	07:18:00	438	71	86	72	97	81
443	07:23:00	443	70	79	74	73	74
448	07:28:00	448	73	57	72	82	71
453	07:33:00	453	74	62	128	66	82
458	07:38:00	458	76	43	109	72	75
463	07:43:00	463	69	57	126	67	80
468	07:48:00	468	83	56	88	92	80
473	07:53:00	473	100	74	66	105	86
478	07:58:00	478	70	63	100	119	88
483	08:03:00	483	66	59	102	94	80
488	08:08:00	488	70	67	86	68	73
493	08:13:00	493	67	51	79	76	68
498	08:18:00	498	79	57	110	66	78
503	08:23:00	503	78	70	71	78	74
508	08:28:00	508	85	85	80	78	80
513	08:33:00	513	69	80	64	62	69
518	08:38:00	518	72	82	117	62	83
523	08:43:00	523	78	68	121	66	83
528	08:48:00	528	74	46	81	88	72
533	08:53:00	533	87	46	80	94	77
538	08:58:00	538	104	79	91	108	95
543	09:03:00	543	104	54	85	100	86
548	09:08:00	548	99	69	76	63	77
553	09:13:00	553	82	63	109	67	80
558	09:18:00	558	66	70	68	78	71
563	09:23:00	563	69	78	73	94	78
568	09:28:00	568	65	50	113	108	84
573	09:33:00	573	90	52	83	100	81
578	09:38:00	578	100	50	71	67	72
583	09:43:00	583	69	86	72	62	72
588	09:48:00	588	74	102	68	61	76
593	09:53:00	593	70	59	70	59	64
598	09:58:00	598	64	53	66	80	66
603	10:03:00	603	69	89	70	97	81
608	10:08:00	608	91	46	70	104	78
613	10:13:00	613	76	31	73	88	67
618	10:18:00	618	101	49	108	70	82
623	10:23:00	623	76	49	136	73	84
628	10:28:00	628	62	58	82	89	73

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
633	10:33:00	633	94	42	69	94	75
638	10:38:00	638	111	82	81	70	86
643	10:43:00	643	77	75	70	62	71
648	10:48:00	648	59	77	72	77	71
653	10:53:00	653	68	73	148	59	87
658	10:58:00	658	101	49	101	60	78
663	11:03:00	663	125	46	89	56	79
668	11:08:00	668	142	68	68	101	95
673	11:13:00	673	150	70	78	128	107
678	11:18:00	678	132	77	92	111	103
683	11:23:00	683	67	33	126	97	81
688	11:28:00	688	62	51	144	101	89
693	11:33:00	693	62	56	116	87	80
698	11:38:00	698	78	21	74	96	67
703	11:43:00	703	144	47	69	102	91
708	11:48:00	708	123	56	85	77	85
713	11:53:00	713	65	71	131	67	84
718	11:58:00	718	112	58	117	77	91
723	12:03:00	723	64	65	105	71	76
728	12:08:00	728	62	59	173	93	97
733	12:13:00	733	76	85	117	79	89
738	12:18:00	738	136	28	74	56	74
743	12:23:00	743	172	50	72	57	88
748	12:28:00	748	153	93	68	61	94
753	12:33:00	753	67	94	65	57	71
758	12:38:00	758	80	67	102	73	80
763	12:43:00	763	73	54	65	104	74
768	12:48:00	768	61	77	65	88	73
773	12:53:00	773	70	84	64	89	77
778	12:58:00	778	120	56	80	91	87
783	13:03:00	783	83	96	138	84	100
788	13:08:00	788	82	99	118	66	91
793	13:13:00	793	63	75	140	91	92
798	13:18:00	798	72	51	125	81	82
803	13:23:00	803	61	54	75	63	63
808	13:28:00	808	61	51	64	63	60
813	13:33:00	813	65	71	70	64	68
818	13:38:00	818	68	84	64	92	77
823	13:43:00	823	71	92	61	100	81
828	13:48:00	828	131	34	64	76	77
833	13:53:00	833	116	49	104	67	84
838	13:58:00	838	64	44	95	61	66

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
843	14:03:00	843	61	62	94	66	71
848	14:08:00	848	57	52	81	55	61
853	14:13:00	853	68	56	71	68	66
858	14:18:00	858	75	49	92	107	81
863	14:23:00	863	69	97	95	66	82
868	14:28:00	868	66	53	67	71	64
873	14:33:00	873	72	32	71	156	83
878	14:38:00	878	65	81	64	113	81
883	14:43:00	883	70	92	65	112	85
888	14:48:00	888	66	52	89	125	83
893	14:53:00	893	77	66	172	117	108
898	14:58:00	898	118	51	161	96	107
903	15:03:00	903	114	79	109	58	90
908	15:08:00	908	71	110	74	62	79
913	15:13:00	913	62	107	71	66	76
918	15:18:00	918	95	62	68	73	75
923	15:23:00	923	93	74	68	113	87
928	15:28:00	928	86	55	72	112	81
933	15:33:00	933	65	48	71	94	70
938	15:38:00	938	60	83	73	90	76
943	15:43:00	943	89	65	73	68	74
948	15:48:00	948	51	30	58	64	53
953	15:53:00	953	55	69	69	60	63
958	15:58:00	958	69	25	66	103	66
963	16:03:00	963	103	62	72	104	85
968	16:08:00	968	85	50	103	90	82
973	16:13:00	973	60	28	98	116	75
978	16:18:00	978	63	106	66	97	83
983	16:23:00	983	156	88	66	86	99
988	16:28:00	988	111	57	94	82	86
993	16:33:00	993	125	96	68	63	88
998	16:38:00	998	132	18	152	61	91
1003	16:43:00	1003	132	65	146	66	102
1008	16:48:00	1008	145	112	85	96	110
1013	16:53:00	1013	124	101	60	109	98
1018	16:58:00	1018	95	89	63	74	80
1023	17:03:00	1023	73	56	66	58	63
1028	17:08:00	1028	66	76	77	120	85
1033	17:13:00	1033	56	49	63	105	68
1038	17:18:00	1038	71	67	130	72	85
1043	17:23:00	1043	69	18	134	61	71
1048	17:28:00	1048	67	36	158	111	93

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
1053	17:33:00	1053	60	83	149	108	100
1058	17:38:00	1058	66	59	143	65	83
1063	17:43:00	1063	82	60	64	108	78
1068	17:48:00	1068	82	51	60	143	84
1073	17:53:00	1073	87	46	54	129	79
1078	17:58:00	1078	122	58	84	115	95
1083	18:03:00	1083	126	30	66	84	76
1088	18:08:00	1088	82	50	61	59	63
1093	18:13:00	1093	64	57	128	59	77
1098	18:18:00	1098	68	57	168	59	88
1103	18:23:00	1103	135	53	163	63	104
1108	18:28:00	1108	85	62	102	77	82
1113	18:33:00	1113	61	55	168	112	99
1118	18:38:00	1118	53	52	146	165	104
1123	18:43:00	1123	58	53	73	152	84
1128	18:48:00	1128	65	38	62	129	74
1133	18:53:00	1133	59	24	63	77	56
1138	18:58:00	1138	104	7	67	121	75
1143	19:03:00	1143	133	8	77	97	79
1148	19:08:00	1148	95	43	69	79	72
1153	19:13:00	1153	146	60	106	85	99
1158	19:18:00	1158	105	63	120	70	91
1163	19:23:00	1163	75	63	133	78	87
1168	19:28:00	1168	64	76	136	93	92
1173	19:33:00	1173	77	64	70	70	70
1178	19:38:00	1178	85	80	59	71	74
1183	19:43:00	1183	59	70	72	70	68
1188	19:48:00	1188	63	85	94	69	78
1193	19:53:00	1193	65	88	109	72	84
1198	19:58:00	1198	88	134	102	62	96
1203	20:03:00	1203	99	122	98	75	99

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
3	00:03:00	3	88	94	136	108	106
8	00:08:00	8	94	148	133	172	136
13	00:13:00	13	113	118	123	174	132
18	00:18:00	18	75	108	132	169	121
23	00:23:00	23	87	72	112	147	105
28	00:28:00	28	84	71	90	146	98
33	00:33:00	33	81	69	85	172	102
38	00:38:00	38	86	66	90	115	89
43	00:43:00	43	97	65	124	75	90
48	00:48:00	48	88	75	124	74	90
53	00:53:00	53	89	79	135	103	101
58	00:58:00	58	84	91	93	124	98
63	01:03:00	63	75	63	117	118	93
68	01:08:00	68	70	61	97	116	86
73	01:13:00	73	75	66	78	70	72
78	01:18:00	78	83	73	80	74	78
83	01:23:00	83	83	74	90	72	80
88	01:28:00	88	84	67	106	73	82
93	01:33:00	93	85	69	91	76	80
98	01:38:00	98	73	75	76	103	82
103	01:43:00	103	76	72	81	74	76
108	01:48:00	108	79	74	87	80	80
113	01:53:00	113	81	66	105	77	83
118	01:58:00	118	85	77	116	73	88
123	02:03:00	123	80	70	79	75	76
128	02:08:00	128	78	70	75	82	76
133	02:13:00	133	77	67	75	78	74
138	02:18:00	138	82	70	94	88	84
143	02:23:00	143	91	71	109	101	93
148	02:28:00	148	88	73	104	110	94
153	02:33:00	153	85	75	94	125	95
158	02:38:00	158	85	74	88	120	92
163	02:43:00	163	74	78	117	115	96
168	02:48:00	168	82	73	94	104	88
173	02:53:00	173	81	80	84	77	80
178	02:58:00	178	82	89	89	83	86
183	03:03:00	183	90	70	88	120	92
188	03:08:00	188	78	56	80	126	85
193	03:13:00	193	86	64	82	95	82
198	03:18:00	198	88	49	84	84	76
203	03:23:00	203	81	51	71	75	70
208	03:28:00	208	78	61	87	72	74

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
213	03:33:00	213	86	60	109	92	87
218	03:38:00	218	94	72	105	104	94
223	03:43:00	223	79	73	78	93	81
228	03:48:00	228	78	69	76	75	74
233	03:53:00	233	85	75	95	84	85
238	03:58:00	238	84	73	102	73	83
243	04:03:00	243	67	61	74	73	69
248	04:08:00	248	84	65	77	72	75
253	04:13:00	253	80	66	81	91	80
258	04:18:00	258	81	66	92	87	81
263	04:23:00	263	74	68	128	78	87
268	04:28:00	268	79	68	99	80	82
273	04:33:00	273	81	85	120	81	92
278	04:38:00	278	80	88	138	96	101
283	04:43:00	283	83	84	91	110	92
288	04:48:00	288	102	81	68	133	96
293	04:53:00	293	92	82	73	94	85
298	04:58:00	298	81	67	73	81	76
303	05:03:00	303	89	89	75	111	91
308	05:08:00	308	83	80	78	116	89
313	05:13:00	313	73	66	101	87	82
318	05:18:00	318	77	63	115	94	87
323	05:23:00	323	74	66	103	115	90
328	05:28:00	328	78	85	81	143	97
333	05:33:00	333	94	104	76	184	114
338	05:38:00	338	83	151	87	115	109
343	05:43:00	343	76	107	68	134	96
348	05:48:00	348	72	87	73	133	91
353	05:53:00	353	89	102	88	141	105
358	05:58:00	358	82	83	125	138	107
363	06:03:00	363	87	60	132	86	91
368	06:08:00	368	97	95	98	120	102
373	06:13:00	373	98	115	77	104	98
378	06:18:00	378	100	108	66	93	92
383	06:23:00	383	75	126	120	85	101
388	06:28:00	388	88	74	110	73	86
393	06:33:00	393	89	63	109	74	84
398	06:38:00	398	69	84	68	143	91
403	06:43:00	403	79	106	87	150	106
408	06:48:00	408	72	141	70	146	107
413	06:53:00	413	77	88	72	153	98
418	06:58:00	418	80	120	104	86	97

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
423	07:03:00	423	81	121	123	80	101
428	07:08:00	428	97	66	141	69	93
433	07:13:00	433	124	69	87	134	103
438	07:18:00	438	105	127	122	127	120
443	07:23:00	443	76	135	132	71	104
448	07:28:00	448	73	96	122	65	89
453	07:33:00	453	86	76	79	77	80
458	07:38:00	458	116	74	71	121	95
463	07:43:00	463	93	66	97	93	87
468	07:48:00	468	105	70	71	67	78
473	07:53:00	473	75	69	101	92	84
478	07:58:00	478	80	103	99	124	101
483	08:03:00	483	71	133	72	140	104
488	08:08:00	488	66	111	77	119	93
493	08:13:00	493	76	127	94	162	115
498	08:18:00	498	69	67	74	129	85
503	08:23:00	503	84	70	76	104	84
508	08:28:00	508	108	72	93	75	87
513	08:33:00	513	117	68	101	104	98
518	08:38:00	518	95	101	95	152	110
523	08:43:00	523	72	120	89	132	103
528	08:48:00	528	74	98	95	109	94
533	08:53:00	533	88	83	68	72	78
538	08:58:00	538	94	66	99	106	91
543	09:03:00	543	74	59	71	97	75
548	09:08:00	548	75	76	68	83	75
553	09:13:00	553	72	66	89	69	74
558	09:18:00	558	77	69	83	72	75
563	09:23:00	563	79	102	75	137	98
568	09:28:00	568	85	101	80	130	99
573	09:33:00	573	75	91	96	125	97
578	09:38:00	578	67	69	74	131	85
583	09:43:00	583	76	68	76	127	87
588	09:48:00	588	91	81	98	90	90
593	09:53:00	593	98	93	93	71	89
598	09:58:00	598	104	66	76	77	81
603	10:03:00	603	74	69	92	100	84
608	10:08:00	608	69	69	114	73	81
613	10:13:00	613	69	93	85	72	80
618	10:18:00	618	87	108	76	70	85
623	10:23:00	623	77	104	78	113	93
628	10:28:00	628	71	102	76	100	87

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
633	10:33:00	633	76	78	106	83	86
638	10:38:00	638	84	71	85	86	82
643	10:43:00	643	97	70	73	78	80
648	10:48:00	648	71	75	101	75	80
653	10:53:00	653	69	85	113	81	87
658	10:58:00	658	84	88	74	82	82
663	11:03:00	663	77	114	88	83	91
668	11:08:00	668	71	127	87	76	90
673	11:13:00	673	74	122	78	78	88
678	11:18:00	678	77	132	100	81	98
683	11:23:00	683	65	83	114	89	88
688	11:28:00	688	70	63	64	85	71
693	11:33:00	693	73	66	76	80	74
698	11:38:00	698	81	68	66	79	73
703	11:43:00	703	81	101	69	89	85
708	11:48:00	708	80	79	120	95	93
713	11:53:00	713	74	70	89	130	91
718	11:58:00	718	74	69	85	128	89
723	12:03:00	723	91	94	68	132	96
728	12:08:00	728	93	121	100	106	105
733	12:13:00	733	67	111	118	81	94
738	12:18:00	738	70	83	87	91	83
743	12:23:00	743	69	72	82	121	86
748	12:28:00	748	92	78	86	100	89
753	12:33:00	753	97	69	98	74	85
758	12:38:00	758	121	68	71	76	84
763	12:43:00	763	70	100	117	70	89
768	12:48:00	768	72	103	72	70	79
773	12:53:00	773	75	116	71	70	83
778	12:58:00	778	71	92	116	138	104
783	13:03:00	783	65	72	106	144	97
788	13:08:00	788	67	88	74	122	88
793	13:13:00	793	70	66	79	134	87
798	13:18:00	798	102	83	70	96	88
803	13:23:00	803	88	76	74	70	77
808	13:28:00	808	72	94	95	72	83
813	13:33:00	813	77	77	63	137	88
818	13:38:00	818	68	93	63	172	99
823	13:43:00	823	72	81	91	133	94
828	13:48:00	828	70	85	77	73	76
833	13:53:00	833	85	63	95	113	89
838	13:58:00	838	77	67	108	82	83

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
843	14:03:00	843	62	69	84	107	80
848	14:08:00	848	68	79	97	158	101
853	14:13:00	853	71	68	68	140	87
858	14:18:00	858	73	71	81	69	74
863	14:23:00	863	107	71	62	69	77
868	14:28:00	868	77	96	74	70	80
873	14:33:00	873	82	69	71	79	75
878	14:38:00	878	67	106	79	146	100
883	14:43:00	883	61	76	119	136	98
888	14:48:00	888	81	65	136	100	96
893	14:53:00	893	73	90	95	68	81
898	14:58:00	898	63	103	73	100	84
903	15:03:00	903	77	110	71	118	94
908	15:08:00	908	77	153	64	72	91
913	15:13:00	913	111	90	109	76	96
918	15:18:00	918	82	134	80	72	92
923	15:23:00	923	76	102	108	139	106
928	15:28:00	928	62	87	78	171	100
933	15:33:00	933	72	59	72	188	97
938	15:38:00	938	65	64	65	94	72
943	15:43:00	943	101	70	68	69	77
948	15:48:00	948	101	60	101	69	83
953	15:53:00	953	92	66	80	113	88
958	15:58:00	958	90	89	66	81	82
963	16:03:00	963	64	113	64	148	97
968	16:08:00	968	68	89	90	114	90
973	16:13:00	973	67	66	105	76	78
978	16:18:00	978	70	66	129	77	85
983	16:23:00	983	67	66	69	129	83
988	16:28:00	988	65	63	67	188	96
993	16:33:00	993	66	64	64	85	70
998	16:38:00	998	70	76	105	66	79
1003	16:43:00	1003	78	96	144	66	96
1008	16:48:00	1008	97	111	108	109	107
1013	16:53:00	1013	65	102	107	179	114
1018	16:58:00	1018	67	63	122	153	101
1023	17:03:00	1023	63	64	119	172	104
1028	17:08:00	1028	66	65	78	128	84
1033	17:13:00	1033	77	70	65	169	95
1038	17:18:00	1038	64	93	69	69	74
1043	17:23:00	1043	58	85	127	71	85
1048	17:28:00	1048	65	67	118	63	78

LUNG SENSITIZATION-DELAYED
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Substance: Desmodur VPPU 1806

Group: 1b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
1053	17:33:00	1053	59	111	64	82	79
1058	17:38:00	1058	68	137	70	77	88
1063	17:43:00	1063	72	139	87	81	95
1068	17:48:00	1068	100	109	125	75	102
1073	17:53:00	1073	88	134	70	75	92
1078	17:58:00	1078	64	163	111	69	102
1083	18:03:00	1083	57	126	68	83	83
1088	18:08:00	1088	59	129	81	71	85
1093	18:13:00	1093	93	81	115	66	89
1098	18:18:00	1098	94	65	103	132	99
1103	18:23:00	1103	61	100	79	183	106
1108	18:28:00	1108	58	125	74	179	109
1113	18:33:00	1113	58	73	131	163	106
1118	18:38:00	1118	140	65	129	200	133
1123	18:43:00	1123	121	65	116	211	128
1128	18:48:00	1128	95	59	74	118	87
1133	18:53:00	1133	59	69	73	64	66
1138	18:58:00	1138	88	63	66	68	71
1143	19:03:00	1143	91	68	78	68	76
1148	19:08:00	1148	87	60	139	72	90
1153	19:13:00	1153	128	62	128	172	123
1158	19:18:00	1158	71	73	89	147	95
1163	19:23:00	1163	62	73	77	176	97
1168	19:28:00	1168	66	74	112	142	99
1173	19:33:00	1173	66	84	77	100	82
1178	19:38:00	1178	74	68	86	70	74
1183	19:43:00	1183	80	82	90	66	80
1188	19:48:00	1188	72	51	84	108	79
1193	19:53:00	1193	60	64	81	144	87
1198	19:58:00	1198	61	65	87	127	85

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Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
3	00:03:00	3	145	102	140	140	132
8	00:08:00	8	91	119	113	104	106
13	00:13:00	13	85	92	84	90	88
18	00:18:00	18	92	106	84	114	99
23	00:23:00	23	95	145	[illegible]	71	100
28	00:28:00	28	107	124	140	109	120
33	00:33:00	33	177	121	108	99	126
38	00:38:00	38	95	93	75	66	82
43	00:43:00	43	89	88	68	79	81
48	00:48:00	48	96	97	77	74	86
53	00:53:00	53	93	121	69	83	92
58	00:58:00	58	104	102	118	105	107
63	01:03:00	63	93	9[illegible]	99	95	95
68	01:08:00	68	83	9[illegible]	70	99	86
73	01:13:00	73	93	8[illegible]	76	77	83
78	01:18:00	78	112	11[illegible]	74	76	93
83	01:23:00	83	73	106	69	80	82
88	01:28:00	88	77	95	94	90	89
93	01:33:00	93	107	89	75	80	88
98	01:38:00	98	95	93	75	74	84
103	01:43:00	103	79	132	75	69	89
108	01:48:00	108	79	98	71	71	80
113	01:53:00	113	64	86	84	109	86
118	01:58:00	118	65	76	62	79	71
123	02:03:00	123	80	80	76	104	85
128	02:08:00	128	93	80	103	94	92
133	02:13:00	133	101	80	152	100	108
138	02:18:00	138	66	76	106	147	99
143	02:23:00	143	67	72	66	131	84
148	02:28:00	148	75	121	86	63	86
153	02:33:00	153	93	144	67	65	92
158	02:38:00	158	71	138	68	85	90
163	02:43:00	163	68	107	80	67	80
168	02:48:00	168	72	110	87	72	85
173	02:53:00	173	109	86	75	110	95
178	02:58:00	178	94	76	63	111	86
183	03:03:00	183	105	85	75	80	86
188	03:08:00	188	90	74	83	68	79
193	03:13:00	193	78	95	88	71	83
198	03:18:00	198	69	111	72	128	95
203	03:23:00	203	75	95	76	133	95
208	03:28:00	208	66	84	96	81	82

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Group: 2a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
213	03:33:00	213	75	85	71	69	75
218	03:38:00	218	77	80	64	59	70
223	03:43:00	223	73	89	73	74	77
228	03:48:00	228	81	81	64	92	80
233	03:53:00	233	85	92	87	121	96
238	03:58:00	238	80	112	120	131	111
243	04:03:00	243	84	105	138	103	108
248	04:08:00	248	82	88	151	61	96
253	04:13:00	253	99	83	120	72	94
258	04:18:00	258	96	88	77	134	99
263	04:23:00	263	58	96	52	136	85
268	04:28:00	268	51	119	93	113	94
273	04:33:00	273	57	133	73	121	97
278	04:38:00	278	74	136	79	61	88
283	04:43:00	283	87	97	79	82	86
288	04:48:00	288	76	102	54	71	76
293	04:53:00	293	112	86	104	61	91
298	04:58:00	298	93	116	74	65	87
303	05:03:00	303	69	118	70	56	78
308	05:08:00	308	77	89	63	55	71
313	05:13:00	313	108	81	90	89	92
318	05:18:00	318	115	82	132	129	116
323	05:23:00	323	82	83	110	142	104
328	05:28:00	328	66	100	73	140	95
333	05:33:00	333	62	101	60	86	77
338	05:38:00	338	64	104	71	88	82
343	05:43:00	343	66	82	70	132	87
348	05:48:00	348	77	80	74	130	90
353	05:53:00	353	87	99	163	76	106
358	05:58:00	358	92	133	129	103	114
363	06:03:00	363	93	126	131	118	117
368	06:08:00	368	140	114	108	68	108
373	06:13:00	373	74	121	98	102	99
378	06:18:00	378	82	109	69	121	95
383	06:23:00	383	99	87	66	140	98
388	06:28:00	388	81	84	66	134	91
393	06:33:00	393	100	83	90	98	93
398	06:38:00	398	139	101	118	63	105
403	06:43:00	403	100	104	87	79	92
408	06:48:00	408	64	108	81	66	80
413	06:53:00	413	72	86	66	79	76
418	06:58:00	418	102	104	90	70	92

LUNG SENSITIZATION-DELAYED
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Group: 2a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
423	07:03:00	423	103	103	92	104	100
428	07:08:00	428	82	115	67	72	84
433	07:13:00	433	69	129	78	59	83
438	07:18:00	438	62	105	65	78	78
443	07:23:00	443	69	88	74	64	74
448	07:28:00	448	98	107	63	71	85
453	07:33:00	453	148	83	65	67	91
458	07:38:00	458	89	82	71	76	79
463	07:43:00	463	67	78	62	82	72
468	07:48:00	468	88	80	69	66	76
473	07:53:00	473	126	86	74	72	89
478	07:58:00	478	92	79	73	97	86
483	08:03:00	483	111	75	68	82	84
488	08:08:00	488	97	86	79	83	86
493	08:13:00	493	92	90	87	133	101
498	08:18:00	498	112	91	74	88	91
503	08:23:00	503	99	78	71	67	79
508	08:28:00	508	109	76	73	81	85
513	08:33:00	513	150	77	78	63	92
518	08:38:00	518	121	91	128	65	101
523	08:43:00	523	75	95	66	74	77
528	08:48:00	528	64	93	73	107	84
533	08:53:00	533	63	82	74	108	81
538	08:58:00	538	58	80	93	71	75
543	09:03:00	543	61	76	104	68	77
548	09:08:00	548	83	85	98	65	83
553	09:13:00	553	97	76	98	64	84
558	09:18:00	558	95	98	66	69	82
563	09:23:00	563	94	94	90	86	91
568	09:28:00	568	57	90	71	69	71
573	09:33:00	573	65	78	68	64	69
578	09:38:00	578	67	75	65	59	67
583	09:43:00	583	70	87	67	89	78
588	09:48:00	588	68	114	107	140	107
593	09:53:00	593	100	110	101	120	108
598	09:58:00	598	122	89	80	67	89
603	10:03:00	603	128	104	72	59	91
608	10:08:00	608	101	76	69	129	94
613	10:13:00	613	81	79	69	135	91
618	10:18:00	618	62	81	73	161	94
623	10:23:00	623	62	113	96	87	89
628	10:28:00	628	63	119	72	56	77

LUNG SENSITIZATION-DELAYED
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Group: 2a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
633	10:33:00	633	61	105	130	116	103
638	10:38:00	638	63	108	141	149	116
643	10:43:00	643	74	101	109	118	100
648	10:48:00	648	119	115	93	87	103
653	10:53:00	653	84	104	65	159	103
658	10:58:00	658	87	112	66	161	107
663	11:03:00	663	123	82	62	62	82
668	11:08:00	668	75	76	170	64	96
673	11:13:00	673	68	79	144	118	102
678	11:18:00	678	65	96	153	167	120
683	11:23:00	683	101	72	126	160	115
688	11:28:00	688	127	72	168	71	110
693	11:33:00	693	64	84	141	64	88
698	11:38:00	698	64	80	113	118	94
703	11:43:00	703	64	73	72	152	90
708	11:48:00	708	79	69	58	131	84
713	11:53:00	713	116	81	66	66	82
718	11:58:00	718	89	80	70	63	76
723	12:03:00	723	60	90	81	67	75
728	12:08:00	728	67	89	63	63	70
733	12:13:00	733	87	109	81	66	86
738	12:18:00	738	117	91	74	60	85
743	12:23:00	743	110	82	63	64	80
748	12:28:00	748	60	85	86	77	77
753	12:33:00	753	57	80	62	66	66
758	12:38:00	758	63	79	64	61	67
763	12:43:00	763	120	80	63	66	82
768	12:48:00	768	94	102	60	58	78
773	12:53:00	773	81	108	65	75	82
778	12:58:00	778	103	114	55	70	86
783	13:03:00	783	87	109	103	65	91
788	13:08:00	788	87	103	96	71	89
793	13:13:00	793	102	77	72	61	78
798	13:18:00	798	87	74	64	138	91
803	13:23:00	803	54	103	61	60	69
808	13:28:00	808	60	101	74	67	76
813	13:33:00	813	67	81	72	82	75
818	13:38:00	818	69	80	69	69	72
823	13:43:00	823	70	99	67	74	77
828	13:48:00	828	77	88	73	60	74
833	13:53:00	833	68	109	83	74	83
838	13:58:00	838	74	104	76	145	100

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Group: 2a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
843	14:03:00	843	114	112	66	160	113
848	14:08:00	848	156	106	74	67	101
853	14:13:00	853	173	102	74	58	102
858	14:18:00	858	161	71	55	60	86
863	14:23:00	863	111	72	86	70	85
868	14:28:00	868	91	86	68	60	76
873	14:33:00	873	86	76	58	142	91
878	14:38:00	878	65	93	53	147	89
883	14:43:00	883	66	83	66	135	87
888	14:48:00	888	63	73	76	80	73
893	14:53:00	893	67	78	116	58	80
898	14:58:00	898	78	81	132	67	90
903	15:03:00	903	70	137	114	62	96
908	15:08:00	908	64	168	77	63	93
913	15:13:00	913	67	150	66	128	103
918	15:18:00	918	78	133	64	187	116
923	15:23:00	923	75	152	55	165	112
928	15:28:00	928	84	123	83	112	101
933	15:33:00	933	156	123	111	95	121
938	15:38:00	938	104	127	90	58	95
943	15:43:00	943	80	128	68	62	85
948	15:48:00	948	64	122	120	78	96
953	15:53:00	953	93	130	115	57	99
958	15:58:00	958	64	144	64	69	85
963	16:03:00	963	70	122	58	166	109
968	16:08:00	968	81	122	60	159	105
973	16:13:00	973	107	96	75	134	103
978	16:18:00	978	201	74	67	161	126
983	16:23:00	983	147	82	87	153	117
988	16:28:00	988	65	87	126	171	112
993	16:33:00	993	87	76	75	142	95
998	16:38:00	998	80	73	76	93	81
1003	16:43:00	1003	60	79	161	54	89
1008	16:48:00	1008	73	109	125	59	92
1013	16:53:00	1013	143	122	76	52	98
1018	16:58:00	1018	185	134	75	87	120
1023	17:03:00	1023	147	127	66	147	122
1028	17:08:00	1028	66	121	69	175	108
1033	17:13:00	1033	62	124	67	199	113
1038	17:18:00	1038	93	91	69	173	107
1043	17:23:00	1043	135	72	71	131	102
1048	17:28:00	1048	80	73	69	132	88

LUNG SENSITIZATION-DELAYED
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Substance: Desmodur VPPU 1806

Group: 2a

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
1053	17:33:00	1053	66	69	81	65	70
1058	17:38:00	1058	66	72	161	60	90
1063	17:43:00	1063	65	128	140	69	100
1068	17:48:00	1068	57	152	135	66	103
1073	17:53:00	1073	58	141	131	58	97
1078	17:58:00	1078	66	130	132	63	98
1083	18:03:00	1083	63	119	86	66	83
1088	18:08:00	1088	93	68	69	66	74
1093	18:13:00	1093	62	75	62	73	68
1098	18:18:00	1098	62	73	58	182	94
1103	18:23:00	1103	156	75	64	96	98
1108	18:28:00	1108	133	80	63	59	84
1113	18:33:00	1113	156	77	64	59	89
1118	18:38:00	1118	175	122	71	81	112
1123	18:43:00	1123	93	146	66	191	124
1128	18:48:00	1128	53	129	109	180	118
1133	18:53:00	1133	58	110	124	95	97
1138	18:58:00	1138	97	126	101	58	96
1143	19:03:00	1143	116	134	91	53	99
1148	19:08:00	1148	94	150	64	60	92
1153	19:13:00	1153	37	81	68	67	63
1158	19:18:00	1158	61	83	75	68	72
1163	19:23:00	1163	59	110	73	99	85
1168	19:28:00	1168	63	87	71	195	104
1173	19:33:00	1173	66	82	68	183	100
1178	19:38:00	1178	72	82	72	143	92
1183	19:43:00	1183	69	72	77	61	70
1188	19:48:00	1188	57	71	89	120	84
1193	19:53:00	1193	54	80	72	65	68
1198	19:58:00	1198	67	95	74	120	89

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
3	00:03:00	3	78	138	88	125	107
8	00:08:00	8	82	130	92	152	114
13	00:13:00	13	84	116	110	87	99
18	00:18:00	18	116	124	101	129	117
23	00:23:00	23	118	126	109	139	123
28	00:28:00	28	108	85	94	105	98
33	00:33:00	33	108	93	88	78	92
38	00:38:00	38	64	134	88	77	91
43	00:43:00	43	66	132	84	79	90
48	00:48:00	48	69	108	86	77	85
53	00:53:00	53	65	124	85	114	97
58	00:58:00	58	80	83	85	128	94
63	01:03:00	63	66	101	82	72	80
68	01:08:00	68	67	94	85	72	80
73	01:13:00	73	72	66	90	71	75
78	01:18:00	78	65	74	45	69	63
83	01:23:00	83	79	81	73	72	76
88	01:28:00	88	84	90	79	80	83
93	01:33:00	93	73	87	83	83	81
98	01:38:00	98	75	93	85	85	84
103	01:43:00	103	91	67	75	75	77
108	01:48:00	108	94	68	68	75	76
113	01:53:00	113	62	74	68	76	70
118	01:58:00	118	86	106	80	79	88
123	02:03:00	123	72	104	82	81	85
128	02:08:00	128	74	113	84	113	96
133	02:13:00	133	93	82	86	141	100
138	02:18:00	138	65	81	88	111	86
143	02:23:00	143	72	78	80	70	75
148	02:28:00	148	100	64	88	71	81
153	02:33:00	153	71	67	89	81	77
158	02:38:00	158	69	95	92	81	84
163	02:43:00	163	70	66	76	69	70
168	02:48:00	168	58	60	84	67	67
173	02:53:00	173	75	97	94	94	90
178	02:58:00	178	68	117	104	137	106
183	03:03:00	183	88	67	87	88	83
188	03:08:00	188	88	65	81	81	79
193	03:13:00	193	92	71	77	102	85
198	03:18:00	198	71	71	83	123	87
203	03:23:00	203	84	80	87	70	80
208	03:28:00	208	82	102	84	71	85

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
213	03:33:00	213	71	116	87	67	85
218	03:38:00	218	74	133	65	67	85
223	03:43:00	223	68	134	76	74	88
228	03:48:00	228	74	117	77	63	83
233	03:53:00	233	63	62	73	64	66
238	03:58:00	238	66	47	81	85	70
243	04:03:00	243	77	65	85	72	75
248	04:08:00	248	99	73	71	68	78
253	04:13:00	253	67	104	72	103	87
258	04:18:00	258	72	65	84	77	75
263	04:23:00	263	110	61	80	99	87
268	04:28:00	268	96	70	72	93	83
273	04:33:00	273	71	68	68	73	70
278	04:38:00	278	80	92	71	115	90
283	04:43:00	283	111	95	85	73	91
288	04:48:00	288	122	76	71	87	89
293	04:53:00	293	93	110	81	69	88
298	04:58:00	298	75	74	77	82	77
303	05:03:00	303	86	65	85	130	91
308	05:08:00	308	118	70	73	128	97
313	05:13:00	313	117	102	97	70	97
318	05:18:00	318	98	110	70	107	96
323	05:23:00	323	67	138	74	72	88
328	05:28:00	328	68	111	89	67	84
333	05:33:00	333	95	127	94	77	98
338	05:38:00	338	134	91	84	89	99
343	05:43:00	343	68	59	92	129	87
348	05:48:00	348	105	110	105	78	100
353	05:53:00	353	140	107	85	100	108
358	05:58:00	358	115	95	87	80	94
363	06:03:00	363	136	128	82	83	107
368	06:08:00	368	134	114	94	106	112
373	06:13:00	373	107	100	97	118	105
378	06:18:00	378	101	74	71	147	98
383	06:23:00	383	77	78	110	134	100
388	06:28:00	388	57	68	101	67	73
393	06:33:00	393	70	99	72	69	77
398	06:38:00	398	91	71	75	64	75
403	06:43:00	403	95	58	76	113	85
408	06:48:00	408	73	66	71	129	85
413	06:53:00	413	79	63	88	106	84
418	06:58:00	418	70	65	78	74	72

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time mih.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
				b/min.			
423	07:03:00	423	110	64	78	73	81
428	07:08:00	428	111	72	93	68	86
433	07:13:00	433	102	88	99	73	91
438	07:18:00	438	79	111	70	79	85
443	07:23:00	443	127	112	66	99	101
448	07:28:00	448	104	104	79	68	89
453	07:33:00	453	103	89	69	63	81
458	07:38:00	458	55	52	83	67	64
463	07:43:00	463	75	58	97	80	78
468	07:48:00	468	64	58	70	66	65
473	07:53:00	473	58	83	71	70	71
478	07:58:00	478	73	100	73	72	80
483	08:03:00	483	63	61	76	75	69
488	08:08:00	488	68	65	96	85	79
493	08:13:00	493	68	76	111	76	83
498	08:18:00	498	79	66	100	67	78
503	08:23:00	503	91	62	80	64	74
508	08:28:00	508	74	82	114	105	94
513	08:33:00	513	118	74	71	84	87
518	08:38:00	518	80	66	78	92	79
523	08:43:00	523	77	60	97	68	75
528	08:48:00	528	65	58	77	66	66
533	08:53:00	533	84	57	95	110	86
538	08:58:00	538	68	110	70	103	88
543	09:03:00	543	72	79	85	124	90
548	09:08:00	548	66	103	67	74	77
553	09:13:00	553	63	150	79	68	90
558	09:18:00	558	57	80	78	71	71
563	09:23:00	563	68	122	102	95	97
568	09:28:00	568	81	98	69	75	81
573	09:33:00	573	65	57	108	75	77
578	09:38:00	578	64	57	97	79	74
583	09:43:00	583	58	60	107	66	73
588	09:48:00	588	70	55	83	72	70
593	09:53:00	593	64	91	74	114	86
598	09:58:00	598	68	138	74	82	90
603	10:03:00	603	74	55	83	65	69
608	10:08:00	608	115	54	87	70	82
613	10:13:00	613	84	59	106	61	78
618	10:18:00	618	67	59	88	67	70
623	10:23:00	623	89	76	73	87	81
628	10:28:00	628	70	59	73	72	68

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
633	10:33:00	633	59	77	85	95	79
638	10:38:00	638	62	109	107	92	93
643	10:43:00	643	60	124	73	60	79
648	10:48:00	648	60	63	74	62	65
653	10:53:00	653	62	70	114	91	84
658	10:58:00	658	63	61	79	153	89
663	11:03:00	663	68	61	66	109	76
668	11:08:00	668	86	79	70	67	75
673	11:13:00	673	85	58	69	71	71
678	11:18:00	678	90	63	100	128	95
683	11:23:00	683	60	61	83	106	78
688	11:28:00	688	66	71	79	93	77
693	11:33:00	693	61	58	75	63	64
698	11:38:00	698	58	83	97	68	77
703	11:43:00	703	58	125	78	80	85
708	11:48:00	708	76	121	71	63	82
713	11:53:00	713	96	79	75	60	77
718	11:58:00	718	103	61	81	77	78
723	12:03:00	723	98	56	81	91	82
728	12:08:00	728	86	123	93	112	103
733	12:13:00	733	55	113	116	122	102
738	12:18:00	738	64	133	78	131	102
743	12:23:00	743	75	104	101	75	89
748	12:28:00	748	69	58	80	63	67
753	12:33:00	753	59	59	104	66	72
758	12:38:00	758	64	62	72	87	71
763	12:43:00	763	85	60	87	114	86
768	12:48:00	768	67	58	87	121	83
773	12:53:00	773	52	63	73	95	71
778	12:58:00	778	73	62	85	65	71
783	13:03:00	783	67	64	76	68	69
788	13:08:00	788	61	63	89	94	77
793	13:13:00	793	71	67	69	95	75
798	13:18:00	798	60	69	72	89	73
803	13:23:00	803	90	113	112	66	95
808	13:28:00	808	97	84	75	67	81
813	13:33:00	813	60	59	68	74	66
818	13:38:00	818	59	61	73	90	71
823	13:43:00	823	67	58	94	138	89
828	13:48:00	828	84	98	72	123	94
833	13:53:00	833	99	117	108	116	110
838	13:58:00	838	59	67	88	62	69

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
843	14:03:00	843	63	62	70	63	65
848	14:08:00	848	83	68	73	70	74
853	14:13:00	853	75	112	67	79	88
858	14:18:00	858	63	59	106	64	73
863	14:23:00	863	65	56	134	155	103
868	14:28:00	868	58	63	147	146	103
873	14:33:00	873	68	57	136	104	91
878	14:38:00	878	69	59	148	73	87
883	14:43:00	883	78	60	80	66	71
888	14:48:00	888	62	60	77	63	66
893	14:53:00	893	66	59	89	57	68
898	14:58:00	898	71	42	73	67	63
903	15:03:00	903	53	111	78	76	79
908	15:08:00	908	52	129	68	110	90
913	15:13:00	913	57	67	73	62	65
918	15:18:00	918	76	91	70	66	76
923	15:23:00	923	113	54	69	58	73
928	15:28:00	928	117	56	83	124	95
933	15:33:00	933	101	78	82	127	97
938	15:38:00	938	53	59	134	151	99
943	15:43:00	943	72	57	102	150	95
948	15:48:00	948	65	114	88	92	89
953	15:53:00	953	57	101	73	93	81
958	15:58:00	958	62	109	74	71	79
963	16:03:00	963	59	135	73	65	83
968	16:08:00	968	48	162	74	76	90
973	16:13:00	973	58	131	92	58	85
978	16:18:00	978	71	138	97	56	91
983	16:23:00	983	135	127	150	65	119
988	16:28:00	988	141	71	148	114	118
993	16:33:00	993	124	51	131	156	116
998	16:38:00	998	115	60	156	139	117
1003	16:43:00	1003	82	57	152	62	88
1008	16:48:00	1008	116	54	87	65	80
1013	16:53:00	1013	45	60	104	55	66
1018	16:58:00	1018	94	64	107	59	81
1023	17:03:00	1023	83	53	62	73	68
1028	17:08:00	1028	46	56	95	118	79
1033	17:13:00	1033	57	86	77	121	85
1038	17:18:00	1038	54	135	69	106	91
1043	17:23:00	1043	51	137	65	127	95
1048	17:28:00	1048	96	54	70	149	92

LUNG SENSITIZATION-DELAYED
Study-no.: T6039897
Substance: Desmodur VPPU 1806

Group: 2b

No.	Time hh:mm:ss	Time min.	RR-1	RR-2	RR-3	RR-4	RR-MEAN
					b/min.		
1053	17:33:00	1053	127	51	73	154	101
1058	17:38:00	1058	73	79	93	69	79
1063	17:43:00	1063	64	97	68	53	70
1068	17:48:00	1068	66	85	81	69	75
1073	17:53:00	1073	58	101	68	79	77
1078	17:58:00	1078	57	63	77	65	66
1083	18:03:00	1083	54	55	73	61	61
1088	18:08:00	1088	65	54	156	61	84
1093	18:13:00	1093	70	64	113	59	77
1098	18:18:00	1098	78	57	71	67	68
1103	18:23:00	1103	98	54	71	64	72
1108	18:28:00	1108	130	90	76	63	90
1113	18:33:00	1113	64	106	124	64	89
1118	18:38:00	1118	52	101	89	62	76
1123	18:43:00	1123	59	110	65	65	75
1128	18:48:00	1128	60	61	65	75	65
1133	18:53:00	1133	64	58	149	166	109
1138	18:58:00	1138	100	86	82	155	106
1143	19:03:00	1143	117	113	65	68	91
1148	19:08:00	1148	85	81	43	54	66
1153	19:13:00	1153	68	58	47	62	59
1158	19:18:00	1158	125	58	73	68	81
1163	19:23:00	1163	100	55	72	73	75
1168	19:28:00	1168	58	55	76	86	69
1173	19:33:00	1173	54	83	74	72	71
1178	19:38:00	1178	55	78	65	69	67
1183	19:43:00	1183	54	61	75	65	64
1188	19:48:00	1188	59	57	67	66	62
1193	19:53:00	1193	55	77	65	67	66
1198	19:58:00	1198	71	161	78	68	94
1203	20:03:00	1203	69	159	89	100	104
1208	20:08:00	1208	68	152	92	67	95
1213	20:13:00	1213	59	140	67	59	81

Gross Pathological Findings

Individual Findings / Guinea Pig ♀

Conc. mg/m³	Animal No.	Time of Death	Sacrificed At	Findings
0	1		25d	Lungs: gelatinous foci
	2		25d	Lungs: gelatinous foci
	3		25d	Lungs: gelatinous, reddish foci
	4		25d	ngl
	5		25d	Lungs: hepatization
	6		25d	Lungs: gelatinous foci
	7		25d	ngl
	8		25d	Lungs: gelatinous foci
MDI Induction	9		25d	Trachea: serous fluid; Lungs: distended and reddish discoloration
	10		25d	Lungs: distended, gelatinous
	11		25d	Lungs: gelatinous foci
	12		25d	Lungs: distended foci
	13		25d	Lungs: distended, reddish foci
	14		25d	Lungs: hepatization
	15		25d	Lungs: distended, gelatinous foci
	16		25d	Lungs: distended; gelatinous foci

ngl = no gross lesions

Prof. Dr. med. U. Mohr
Director of the Institute of Experimental Pathology
Medizinische Hochschule Hannover
[Hannover School of Medicine]

3000 Hannover 61
Konstanty-Gutschow-Strasse 8
Tel.: (05 11) 5 32 45 20
Telex: 9 22 044
9 22 044 medho d

Institute of Toxicology
BAYER AG - Elberfeld Works
Fr.-Ebert-Str. 217
5600 Wuppertal-Elberfeld

December 19, 1991

DESMODUR VP PU 1806
Study of the Lung Sensitization of Guinea Pigs
Study No. T6039897 (3552)

Pathology Report

1. Materials and Methods

The guinea pigs were necropsied at the Institute of Toxicology of BAYER AG and examined grossly. The gross pathological findings from the necropsy records were accepted and integrated into this report.

Tissues, fixed in formalin, from 16 female guinea pigs (induced with DESMODUR VP PU 1806 or vehicle) of the strain BOR:DHPW were submitted for histopathological examination. The guinea pigs had been sacrificed under diethyl ether anesthesia following a DESMODUR VP PU 1806 aerosol challenge and the accompanying physiological examination for immediate and delayed reactions.

The guinea pigs were assigned to the groups as follows:

Group	Animal No.*	Sex	Induction	Survival Time
1.	001001 - 001008	Female	Control	25 days
2.	002009 - 002016	Female	DESMODUR VP PU 1806	25 days

* Animal No. designation for the statistical evaluation of histopathological findings.

The histological sections were prepared by Experimental Pathology Services (U.K.) Ltd., Hereford, England.

The organs/tissues to be examined were first irrigated, then embedded in Paramat wax after trimming, and sections for each organ or tissue were prepared; the average thickness was 5 µm (minimum 4 µm, maximum 7 µm). The sections were stained with hematoxylin and eosin (H&E) by the method of LILLI-MEYER.

Histological slides prepared from the following organs were available for examination:

Trachea, lungs.

2. Gross Pathological Findings

The following findings were observed in some of the control animals and all of the DESMODUR VP PU 1806-induced guinea pigs:

Lungs: distended in some cases, and with reddish, gelatinous, and/or hepatoid foci in some cases.

Histopathological correlation: peripheral emphysema, hyperemia, focal eosinophilia in the parenchyma, and/or bronchiolo-alveolar proliferation.

Statistical assessment of the histopathological correlations with these gross findings indicated no significance.

3. Histopathological Findings

Trachea

In the controls and in the DESMODUR VP PU 1806-induced animals, eosinophilic granulocytes were observed in the epithelial region in various degrees of severity.

Lungs

In addition to slight hyperemia, the common peribronchial and perivascular round cell infiltration as well as a bronchiolo-alveolar proliferation, a focal peripheral emphysema was observed primarily in the animals induced with DESMODUR VP PU 1806. A somewhat more severe focal eosinophilia in the parenchyma was also observed in these animals.

4. Summary

Histopathological examination revealed a more severe eosinophilia (focal eosinophilic granulocytes in the parenchyma) in the guinea pigs induced with DESMODUR VP PU 1806 than in the control. However, statistical assessment revealed no significant differences.

The individual findings are presented in the Individual Animal Reports and the calculated incidences in the attached Incidence Reports (P.L.A.C.E.S. Program, APOLOCO).

[signed]
(Prof. Dr. med. U. Mohr)

Attachments

Medizinische Hochschule Hannover
[Hannover School of Medicine]
Institute of Experimental Pathology
Prof. Dr. med. U. Mohr
Center for Pathology and Forensic Medicine

MHH - Exp. Pathology - Postfach 6, 01 80 - D-3000 Hannover 61 - Germany

Institute of Toxicology
BAYER AG - Elberfeld Works
Fr.-Ebert-Str. 217
5600 Wuppertal-Elberfeld

My Reference: 5120

December 21, 1991

STATEMENT

DESMODUR VP PU 1806

Study No. T6039897 (3552)

Study of the Lung Sensitization of Guinea Pigs

The report tables were prepared with the necessary thoroughness and were compared with the individual animal data.

[signed]
Dr. M.B. Ketkar
Person responsible for
Quality Assurance

[signed]
Petra Schneiderheinze

Declaration by Quality Assurance Unit

Study-No.: T 6039897 (3552)

Test Article: Desmodur VP PU 1806

Title of final report:

Desmodur VP PU 1806
Studien-Nr. T 6039897 (3552)
Lungensensibilisierungsstudie an Meerschweinchen
Histopathologische Untersuchung

This report describes the methods and procedures used in the histopathological evaluation and the documented results accurately reflect the raw data of the study.

Hannover, 21.12.1991

M. B. Ketkar

Dr. M. B. Ketkar
Quality Assurance Officer

Declaration by Quality Assurance Unit

Study-No.: T 6039897 (3552)

Test Article: Desmodur VP PU 1806

Title of final report:

Desmodur VP PU 1806
Studien-Nr. T 6039897 (3552)
Lungensensibilisierungsstudie an Meerschweinchen
Histopathologische Untersuchung

The conduct of this study has been subjected to one inspection and the findings reported to the pathologist. The date of this inspection is given below.

Date of Q.A. Inspection: 10.05.91

Hannover, 21.12.1991

M B. Ketkar
Dr. M. B. Ketkar
Quality Assurance Officer

QUALITY ASSURANCE UNIT

RCC, Registration and Consulting Company AG, 4452 Itingen Switzerland

S T A T E M E N T

The facilities of Experimental Pathology Services (UK) Limited and the procedures used by them were periodically inspected in accordance with the RCC - Quality Assurance Unit Standard Operating Procedures and the findings were reported to their Management.

Date of last inspection : Jan. 17. 1991

Date of last report to the Management of EPS UK : Jan. 17. 1991

RCC, Quality Assurance Manager: K. Schneider

.....

Date : Jan. 18. 1991

Study Name:	MOHR 62
PLACES input:	Hill
- Date	May 2, 1991
- Incidence Report	May 7, 1991
- Correction	December 18, 1991
Substance:	DESMODUR VP PU 1806
Study No.:	T6039897 (3552)
Animal species:	Female guinea pigs BOR:DHPW
Treatment:	Aerosol inhalation to determine lung sensitization
Groups:	2 (1 control group and 1 treatment group, 8 guinea pigs each)
Number of animals:	16

Report Title

INCIDENCE REPORT

DESMODUR VP PU 1806
Study No. T6039897 (3552)
Histopathological Findings

Group	Animal No.*	Sex	Induction
1.	001001 - 001008	Female	Control
2.	002009 - 002016	Female	DESMODUR VP PU 1806

* Animal No. designation for the statistical evaluation of histopathological findings.

Organs:

Trachea
Lungs

Staining:
H&E all slides

Reports - P.L.A.C.E.S. Program

1. Study data
2. Tissue check sheet
3. Statistics of histopathological findings
   - Incidence of lesions (numeric)
4. Histopathological findings
   - Incidence of lesions (animal Nos.)
5. Individual Animal Reports
   - Gross and histological findings

All printouts with date and page number.

In duplicate (1 original + 1 copy).

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Statistics of histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)													
		0	Des. VP PU 1806												
TRACHEA:		(8)	(8)												
Eosinophilia															
slight		3	2												
moderate		4	4												
severe		1	2												
Multifocal round-cell infiltration															
slight		1	0												

Figures in brackets represent the number of animals from which this tissue was examined microscopically
Significance of differences in a pairwise (Fisher's) test between each treatment and control incidence: * P<0.05, ** P<0.01

INCIDENCE REPORT
Desmodur VP [illegible] 1806
Study-No. T 6039897 (3552)
Statistics of histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)														
		0	Des. VP PU 1806													
LUNGS:		(8)	(8)													
Hyperaemia																
slight		3	6													
moderate		0	1													
Peribronchial round-cell infiltration																
slight		8	8													
Perivascular round-cell infiltration																
slight		5	6													
Eosinophilia																
slight		5	2													
moderate		0	3													
severe		2	2													
Thickening of the septa		0	2													
Marginal emphysema		4	8													

Figures in brackets represent the number of animals from which this tissue was examined microscopically
Significance of differences in a pairwise (Fisher's) test between each treatment and control incidence: * P<0.05, ** P<0.01

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Statistics of histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)	
		0	Des. VP PU 1806
LUNGS:		(8)	(8)
Bronchiolar/alveolar proliferation		8	8
Foreign-body granuloma		0	4
Foreign body giant cell(s)		0	1

Figures in brackets represent the number of animals from which this tissue was examined microscopically
Significance of differences in a pairwise (Fisher's) test between each treatment and control incidence: * P<0.05, ** P<0.01
T 6039897 (3552) (study in progress)

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (ANIML NOS)														
		0	Des. VP PU 1806													
TRACHEA:		(8)	(8)													
Eosinophilia																
	slight	10010041002010														
		10010071002014														
		1001008														
		3/ 8	2/ 8													
	moderate	10010021002009														
		10010031002011														
		10010051002012														
		10010061002015														
		4/ 8	4/ 8													
	severe	10010011002013														
			1002016													
		1/ 8	2/ 8													
Multifocal round-cell infiltration																
	slight	1001007														

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YY (on two lines) are the number of animals listed/number of animals examined.

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

		FEMALES : INCIDENCE OF LESIONS (ANIML NOS)												
LESIONS	TREATMENT	0	Des. VP PU 1806											
TRACHEA:		(8)	(8)											
Multifocal round-cell infiltration		1/ 8	0/ 8											

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YYY (on two lines) are the number of animals listed/number of animals examined.

T 6039897 (3552) (study in progress)

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (ANIML NOS)												
		0	Des. VP PU 1806											
LUNGS:		(8)	(8)											
Hyperaemia														
	slight	100100	310020091											
		100100	710020101											
		100100	810020121											
			10020131											
			10020141											
			10020151											
		3/ 8	6/ 8											
	moderate		10020111											
		0/ 8	1/ 8											
Peribronchial round-cell infiltration														
	slight	100100	110020091											
		100100	210020101											
		100100	310020111											
		100100	410020121											

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YYY (on two lines) are the number of animals listed/number of animals examined.

T 6039897 (3552) (study in progress)

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (ANIML NOS)													
		0	Des. VP PU 1806												
LUNGS:		(8)	(8)												
Peribronchial round-cell infiltration															
slight		1	2												
		1	2												
		1	2												
		1	2												
		8/ 8	8/ 8												
Perivascular round-cell infiltration															
slight		1	1												
		1	2												
		1	2												
		1	2												
		1	2												
			2												
		5/ 8	6/ 8												

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YYY (on two lines) are the number of animals listed/number of animals examined.

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (ANIML NOS)														
		0	Des. VP PU 1806													
LUNGS:		(8)	(8)													
Eosinophilia																
slight		1	0	0	1	0	0	2	1	0	0	2	0	1	2	1
		1	0	0	3	1	0	2	1	0	0	2	0	1	6	1
		1	0	0	4	1										
		1	0	0	6	1										
		1	0	0	7	1										
		5/	2/													
		8	8													
Parenchymal eosinophilia																
moderate			1	0	0	2	1	0	1	1						
			1	0	0	2	1	1	1	1						
			1	0	0	2	1	3	1	1						
		0/	3/													
		8	8													
severe		1	0	0	1	1	0	0	2	0	0	9	1			
		1	0	0	5	1	0	0	2	0	1	4	1			
		2/	2/													
		8	8													

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YY (on two lines) are the number of animals listed/number of animals examined.

T 6039897 (3552) (study in progress)

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (ANIML NOS)												
		0	Des. VP PU 1806											
LUNGS:		(8)	(8)											
Thickening of the septa			0020121											
			0020151											
		0/ 8	2/ 8											
Marginal emphysema		0010041	0020091											
		0010061	0020101											
		0010071	0020111											
		0010081	0020121											
			0020131											
			0020141											
			0020151											
			0020161											
		4/ 8	8/ 8											
Multifocal bronchiolar/alveolar proliferation		0010011	0020091											
		0010021	0020101											
		0010031	0020111											
		0010041	0020121											
		0010051	0020131											

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YYY (on two lines) are the number of animals listed/number of animals examined.

T 6039897 (3552) (study in progress)

INCIDENCE REPORT
Desmodur VP PU 1806
Study-No. T 6039897 (3552)
Histopathological findings

LESIONS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (ANIML NOS)														
		0	Des. VP PU 1806													
LUNGS:		(8)	(8)													
Multifocal bronchiolar/alveolar proliferation		1001006 1001007 1001008 8/ 8	1002014 1002015 1002016 8/ 8													
Focal foreign-body granuloma			1002009 1002013 1002014 3/ 8													
Multifocal foreign-body granuloma			1002010 1/ 8													
Foreign body giant cell(s)			1002009 1/ 8													

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified
Figures in the format XX/YYY (on two lines) are the number of animals listed/number of animals examined.

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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001001		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Gelatinous foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Severe eosinophilia
LUNGS :		
		Multifocal bronchiolar/alveolar proliferation
		Slight peribronchial round-cell infiltration
		Severe focal parenchymal eosinophilia
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001002		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Gelatinous foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Moderate eosinophilia
LUNGS :		
		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Multifocal bronchiolar/alveolar proliferation
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001003		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Gelatinous foci
		Red foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Moderate eosinophilia
LUNGS :		
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

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Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001004		Killed
		Necropsied on Day: 25 Days
GENERAL COMMENTS :		No macroscopic abnormality detected
		MICROSCOPIC FINDINGS
TRACHEA :		Slight eosinophilia
LUNGS :		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Focal marginal emphysema
ALL ORGANS :		Stained H & E
PATHOLOGIST (HISTO-) :		PROF. DR. MOHR
		Data input: HILL

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Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	- MACROSCOPIC & MICROSCOPIC FINDINGS
001005	Killed
	Necropsied on Day: 25 Days
	NECROPSY FINDINGS
LUNGS :	
	Partly hepatoid
	MICROSCOPIC FINDINGS
TRACHEA :	
	Moderate eosinophilia
LUNGS :	
	Multifocal bronchiolar/alveolar proliferation
	Slight peribronchial round-cell infiltration
	Severe focal parenchymal eosinophilia
ALL ORGANS :	
	Stained H & E
PATHOLOGIST (HISTO-) :	
	PROF. DR. MOh.
	Data input: HILL

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Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001006		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Gelatinous foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Moderate eosinophilia
LUNGS :		
		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Focal marginal emphysema
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

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Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001007		Killed
		Necropsied on Day: 25 Days
GENERAL COMMENTS :		No macroscopic abnormality detected
		MICROSCOPIC FINDINGS
TRACHEA :		Slight multifocal round-cell infiltration
		Slight eosinophilia
LUNGS :		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Slight focal marginal emphysema
ALL ORGANS :		Stained H & E
PATHOLOGIST (HISTO-) :		PROF. DR. MOHR
		Data input: HILL

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Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 control 0 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
001008		:led
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Gelatinous foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Slight eosinophilia
LUNGS :		
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Slight focal marginal emphysema
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report

ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002009		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
TRACHEA :		
		Serous fluid within trachea
LUNGS :		
		Distended
		Partly reddish discoloured
		MICROSCOPIC FINDINGS
TRACHEA :		
		Moderate eosinophilia
		No microscopic evidence of macroscopic finding
LUNGS :		
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Severe focal parenchymal eosinophilia
		Multifocal bronchiolar/alveolar proliferation
		Focal foreign-body granuloma
		Foreign body giant cell(s)
		Focal marginal emphysema
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report

ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002010		Killed Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		Distended Gelatinous
		MICROSCOPIC FINDINGS
TRACHEA :		Slight eosinophilia
LUNGS :		Slight focal hyperaemia Slight peribronchial round-cell infiltration Moderate focal parenchymal eosinophilia Slight perivascular round-cell infiltration Multifocal bronchiolar/alveolar proliferation Multifocal foreign-body granuloma Focal marginal emphysema
ORGANS :		Stained H & E
PATHOLOGIST (HISTO-) :		PROF. DR. MOHR Data input: HILL

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Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	- MACROSCOPIC & MICROSCOPIC FINDINGS
002011	Killed
	Necropsied on Day: 25 Days
	NECROPSY FINDINGS
LUNGS :	
	Gelatinous foci
	MICROSCOPIC FINDINGS
TRACHEA :	
	Moderate eosinophilia
LUNGS :	
	Moderate focal hyperaemia
	Slight peribronchial round-cell infiltration
	Moderate focal parenchymal eosinophilia
	Multifocal bronchiolar/alveolar proliferation
	Focal marginal emphysema
ALL ORGANS :	
	Stained H & E
PATHOLOGIST (HISTO-) :	
	PROF. DR. MOHR
	Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002012		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Distended foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Moderate eosinophilia
LUNGS :		
		Focal thickening of the septa
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Slight focal marginal emphysema
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-)	:	
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002013		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Distended and reddish foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Severe eosinophilia
LUNGS :		
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Moderate focal parenchymal eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Focal marginal emphysema
		Foreign-body granuloma
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002014		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Hepatoid foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Slight eosinophilia
LUNGS :		
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Severe focal parenchymal eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Focal marginal emphysema
		Foreign-body granuloma
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
FUER
TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report
ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002015		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Distended and gelatinous foci
		MICROSCOPIC FINDINGS
TRACHEA :		
		Moderate eosinophilia
LUNGS :		
		Focal thickening of the septa
		Slight focal hyperaemia
		Slight peribronchial round-cell infiltration
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferatior
		Focal marginal emphysema
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

FRAUNHOFER INSTITUT
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TOXIKOLOGIE UND AEROSOLFORSCHUNG (ITA)

Individual Animal Report

ATTACHMENT - INDIVIDUAL ANIMAL DATA (CONTINUED)

STUDY NUMBER: T 6039897 (3552) (study in progress)
DOSE GROUP: T 6039897 Desmodur VP PU 1806 Des. VP PU 1806 FEMALES

ANIMAL NO.	-	MACROSCOPIC & MICROSCOPIC FINDINGS
002016		Killed
		Necropsied on Day: 25 Days
		NECROPSY FINDINGS
LUNGS :		
		Gelatinous foci
		Partly distended
		MICROSCOPIC FINDINGS
TRACHEA :		
		Severe eosinophilia
LUNGS :		
		Slight peribronchial round-cell infiltration
		Slight eosinophilia
		Slight perivascular round-cell infiltration
		Multifocal bronchiolar/alveolar proliferation
		Focal marginal emphysema
ALL ORGANS :		
		Stained H & E
PATHOLOGIST (HISTO-) :		
		PROF. DR. MOHR
		Data input: HILL

*** LISTING COMPLETE ***

ALTROMIN STANDARD-DIÄTEN
TOTAL-PATHOGEN-FREI-TPF®

3020

Maintenance Diet Guinea Pigs

Rohnährstoffe*	Nutrients*	
Rohprotein	Crude protein	18,0
Rohfett	Crude fat	5,0
Rohfaser	Crude fiber	14,5
Asche	Ash	8,5
Wasser	Moisture	12,0
N-freie Extraktstoffe	Nitrogen-free extract	42,1

Umsetzbare Energie[2]	Metabolizable Energy[2]	
kcal/kg	kcal/kg	2.450,0
MJ/kg	MJ/kg	10,2

Mineralstoffe*	Minerals*	
Calcium	Calcium	0,9
Phosphor	Phosphorus	0,7
Magnesium	Magnesium	0,2
Natrium	Sodium	0,2
Kalium	Potassium	1,5

Aminosäuren*	Amino Acids*	
Lysine		0,90
Methionine		0,35
Cystine		0,25
Phenylalanine		0,70
Tyrosine		0,60
Arginine		1,00
Histidine		0,40
Tryptophane		0,20
Threonine		0,70
Isoleucine		0,80
Leucine		1,40
Valine		0,90

Spurenelemente**	Trace elements**	
Mangan	Manganese	60,0
Eisen	Iron	165,0
Kupfer	Copper	16,0
Zink	Zinc	50,0
Jod	Iodine	0,9
Fluor	Fluorine	10,0

Vitamine***	Vitamins***	Standard Diet		Standard Diet fortified	
Vitamin A	Vitamin A	15.000,0	IU	25.000,0	IU
Vitamin D	Vitamin D	600,0	IU	1.000,0	IU
Vitamin E	Vitamin E	75,0	mg	125,0	mg
Vitamin K	Vitamin K	3,0	mg	5,0	mg
Vitamin B_1	Vitamin B_1	18,0	mg	30,0	mg
Vitamin B_2	Vitamin B_2	12,0	mg	20,0	mg
Vitamin B_6	Vitamin B_6	9,0	mg	15,0	mg
Vitamin B_{12}	Vitamin B_{12}	24,0	mcg	40,0	mcg
Nikotinsäure	Nicotinic acid	36,0	mg	60,0	mg
Pantothensäure	Pantothenic acid	21,0	mg	35,0	mg
Folsäure	Folic acid	2,0	mg	3,0	mg
Biotin	Biotin	60,0	mcg	100,0	mcg
Cholin	Choline	600,0	mg	1.000,0	mg
Vitamin C	Vitamin C	1.036,0	mg	1.060,0	mg

* % in der Diät (Mittelwert) / average % content in the diet
** mg in 1 kg Diät (Mittelwert) / average mg content in 1 kg diet
*** Zusatz in 1 kg Diät / additive in 1 kg diet
1) EG-Empfehlung / EC recommended
2) berechnet / calculated

ALTROMIN Standard-Diäten garantieren größte Sicherheit bei Versuchen
ALTROMIN Standard Diets warrant experimental safety

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ALTROMIN STANDARD-DIÄTEN
TOTAL-PATHOGEN-FREI-TPF®

3020

Haltungsdiät Meerschweinchen

Langjährige Erfahrung empfiehlt ALTROMIN 3020 Haltungsdiät für Meerschweinchen als Alleindiät ohne Einschränkung für die Phase der Haltung ausgewachsener Tiere ab einem Lebensalter von zehn Wochen. Diese Haltungsdiät wird zur freien Aufnahme angeboten. Stetige Frischwasserversorgung ist zu sichern.
In Plastiksäcke verschweißt, ist ALTROMIN 3020 direkt zum Einschleusen in SPF-Bereiche geeignet. Dafür ist lediglich eine Oberflächendesinfektion des verschweißten Plastiksackes erforderlich (z. B. Tauchbad).

ALTROMIN 3020 Guinea Pig Maintenance Diet is an established maintenance diet for animals of ten weeks and older. The diet should be offered ad libitum together with an ample supply of fresh water.
Sealed in polyethylene lined sacks, ALTROMIN 3020 can be passed directly into the SPF facility following surface disinfection.

Haltungstemperatur/room temperature 20 - 24° C[1]

relative Luftfeuchtigkeit/relative humidity 50-60%

Futteraufnahme g/Tag / Food absorption g/day

	Wachstum / growth phase	erwachs. Tiere / adult
Meerschweinchen / Guinea Pigs	bis 50 g	ca. 60 g

ALTROMIN 3020 ist lieferbar:
ALTROMIN 3020 is available as:

	Mehl/Powder	3021
3,0 mm	Preßlinge/Pellets	3022
15,0 mm	Preßlinge/Pellets	3025

ALTROMIN Standard-Diäten - das Produkt jahrelanger Erfahrung
ALTROMIN Standard Diets - the result of long years' experience

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Futterspezifikation
Specification of Feed

BAYER AG
FACHBEREICH TOXIKOLOGIE

DESMODUR VP PU 1805

T6038897

Futterspezifikation
Specification of Feed

Impurity	Max. acceptable value	LUFA - Limit of detection	Altromin *
Aflatoxine B_1 / B_2	0,01	0,0025	nng
Aflatoxine G_1 / G_2	0,01	0,0025	nng
Antibiotic activity	± 0		nng
Arsenic	2,0	0,2	0,3
Fluoride	150,0	5,0	22,0
Mercury	0,1	0,01	0,08
Lead	5,0	0,1	0,37
Cadmium		0,01	0,10
Selenium		0,10	1,0
Tecnazene		0,001	< 0,001
Quintozene		0,001	< 0,001
HCB (Hexachlorbenzene)		0,001	< 0,001
α - HCH		0,001	< 0,001
β - HCH		0,002	< 0,002
γ - HCH	0,1	0,001	0,002
Heptachlor	0,03	0,005	< 0,005
Heptachlorepoxid	0,03	0,005	< 0,005
α - Chlordan	0,05	0,005	< 0,005
γ - Chlordan	0,05	0,005	< 0,005
Aldrin	0,02	0,005	< 0,005
Dieldrin	0,02	0,005	< 0,005
Endrin	0,02	0,01	< 0,01
o,p - DDE	0,05	0,005	< 0,005
p,p - DDE	0,05	0,005	< 0,005
o,p - DDD	0,05	0,005	< 0,005
o,p - DDT	0,05	0,005	< 0,005
p,p - DDD	0,05	0,01	< 0,01
p,p - DDT	0,05	0,01	< 0,01
Methoxychlor		0,01	< 0,01
PCB qual,			nng
Chlorthion		0,01	< 0,01
Disulfothion		0,005	< 0,005
Malathion		0,01	< 0,01
Methylparathion		0,005	< 0,005
Ethylparathion		0,01	< 0,01
Sulfotepp		0,002	< 0,002
Fenthion		0,005	< 0,005
Diazinon		0,01	< 0,01
Dibrom		0,02	< 0,02
Dimethoate		0,005	< 0,005
Trichlorphon		0,01	< 0,01
Fenitrothion		0,01	< 0,01

* In this study Altromin 1324 was used.
4 is the degree of pelletation.

Dimension: ppm

Wasserspezifikation
Specification of Water

No	Substance	Limit mg/l	computed as	equivalent $mmol/m^3$	acceptable error of value (± mg/l)
1	Arsenic	0,04	As	0,5	0,015
2	Lead	0,04	Pb	0,2	0,02
3	Cadmium	0,005	Cd	0,04	0,002
4	Chrome	0,05	Cr	1	0,01
5	Cyanide	0,05	CN^-	2	0,01
6	Fluoride	1,5	F^-	79	0,2
7	Nickel	0,05	Ni	0,9	0,01
8	Nitrate	50	NO_3^-	806	2
9	Nitrite	0,1	NO_2^-	2,2	0,02
10	Mercury	0,001	Hg	0,005	0,0005
11	Polycyclic aromatic carbohydrates - Fluoranthene - Benzo-b-fluoranthene - Benzo-a-pyrene - Benzo-(ghi)-perylene - Indeno-(1,2,3-cd)-pyrene	0,0002	C	0,02	0,00004
12	Organochloric compounds - 1,1,1-Trichlorethane Trichlorethylene Tetrachlorethylene Dichlormethane	0,025	-	-	0,01
	- Tetrachlormethane	0,003	CCl_4	0,02	0,001

DESMODUR VP PU 1806 Specifications

Final Report

IDENTITY CHECK AND ANALYTICAL ACCOUNTABILITY

BAYER AG
ZF-D/Central Analytical
Bldg. O 13
5090 Leverkusen, Germany

DATE : MARCH 28, 1991
STUDY NO. : G 90/0158/00 LEV
STUDY DIRECTOR : Dr. Kausler
REPRESENTATIVE : Dr. Kassühlke

Test Substance:	DESMODUR VP PU 1806		
Requested by:	Dr. Pilger, PU-S/UP LEV Bldg. B 211	Request No.:	--
Chemical name:	Diisocyanatodiphenylmethane		
Empirical formula:	$C_{15}H_{10}N_2O_2$	Molecular Weight:	250.3
CAS Name:	--		
CAS No.:	--		
Product No.:	417 297 02		
Batch/Batch No.:	001326 F 072		
Sample No.:	180532/90	Shipment date:	Nov. 12, 1990
Manufacturing plant:	PU	Date manufactured:	Feb. 14, 1990
Start of study:	January 30, 1991	Stable through:	Nov. 12, 1991
End of study:	March 19, 1991		

1. Description of Methods and Individual Results

1.1 Identity check
SOP : CIR0004801
Laboratory supervisor: Dr. Seelemann
Results : pass

1.2 Tests for compliance with specifications and additional tests for accountability
Specification dated : --
Specification data : --

1.2.1 Test : Uretdion content
Method No. : 2079/078/180/91
Laboratory supervisor: Dr. Seelemann
Results : 0.10% uretdion

1.2.2 Test : Phenyl isocyanate (GC)
Method No. : 2079/078/180/88 K
Laboratory supervisor: Dr. Schödel
Results : not detectable < 1 mg/kg phenyl isocyanate

1.2.3 Test : Total chlorine
Method No. : 2088/162/030/54
Laboratory supervisor: Dr. Mauss
Results : < 0.0010% chlorine

IDENTITY CHECK AND ANALYTICAL ACCOUNTABILITY

BAYER AG
ZF-D/Central Analytical
Bldg. O 13
5090 Leverkusen, Germany

DATE : MARCH 28, 1991
STUDY NO. : G 90/0158/00 LEV
STUDY DIRECTOR : Dr. Kausler
REPRESENTATIVE : Dr. Kassühlke

Test Substance: DESMODUR VP PU 1806

Requested by: Dr. Pilger, PU-S/UP LEV Bldg. B 211 Request No.: --

1.2.4 Test : Hydrolyzable chlorine
Method No. : 2076/078/010/09
Laboratory supervisor: Dr. Fus
Results : 0.0004% hydrolyzable chlorine

1.2.5 Test : Purity using dibutylamine titration
Method No. : 2076/078/010/11
Laboratory supervisor: Dr. Fus
Results : 99.4% / 99.4% purity (based on MW = 250.3)

1.2.6 Test : Isomer separation (GC)
Method No. : 2086/078/180/107
Laboratory supervisor: Dr. Kausler
Results : GC (vaporized substance = 100%)

0.2% 2,2'-diisocyanatodiphenylmethane
51.2% 2,4'-diisocyanatodiphenylmethane
48.5% 4,4'-diisocyanatodiphenylmethane
0.1% unknown compound

1.2.7 Test : Content and impurities (GC)
Method No. : K2011-0163601-91D
Laboratory supervisor: Dr. Kausler
Results :
GC (vaporized substance = 100% - % uretdion)

0.2% 2,2'-diisocyanatodiphenylmethane
51.2% 2,4'-diisocyanatodiphenylmethane
48.3% 4,4'-diisocyanatodiphenylmethane
0.2% unknown compounds
4 impurities

1.3 Material Accountability

0.1 % uretdion
0.2 % 2,2'-diisocyanatodiphenylmethane
51.2 % 2,4'-diisocyanatodiphenylmethane
48.3 % 4,4'-diisocyanatodiphenylmethane
0.2 % unknown compounds

100.0% total

IDENTITY CHECK AND ANALYTICAL ACCOUNTABILITY

BAYER AG
ZF-D/Central Analytical
Bldg. O 13
5090 Leverkusen, Germany

DATE : MARCH 28, 1991
STUDY NO. : G 90/0158/00 LEV
STUDY DIRECTOR : Dr. Kausler
REPRESENTATIVE : Dr. Kassühlke

Test Substance: DESMODUR VP PU 1806

Requested by: Dr. Pilger, PU-S/UP LEV Bldg. B 211 Request No.: --

2. **Assessment and Comments**
- Material accountability is complete according to the current state of the art.
- Raw data have been audited and archived.

3. **Statement**
The study was performed in compliance with the OECD Principles of Good Laboratory Practice (GLP).

4. **Archiving**
The study protocol and the other study documentation are stored in the archives of ZF-DZA/OAL, BAYER AG, Leverkusen, Bldg. O 13.

Leverkusen, March 28, 1991 Study Director: [signed: Kausler]

Laboratory Supervisors: (Dr. Seelemann): [signed]
(Dr. Schödel): [signed]
(Dr. Mauss): [signed]
(Dr. Fus): [signed]

Attachments: Quality Assurance Statement (QAU)

Distribution: Dr. Pilger, PU-S/UP LEV, Bldg. B 211
Archives
Laboratory Supervisors
QAU
ZF-DZA, Coordination of Old and New Materials Analysis
Dr. Kausler

BAYER AG
ZF-DZA/Analytical Leverkusen/OAL
Leverkusen Works, Bldg. O 13
D-5090 Leverkusen, Germany

Quality Assurance Statement -- Final Report

Study No. or Request No.: G90/0158/00 LEV
Title of the GLP Study: Characterization/Material Accountability of DESMODUR VP PU 1806

This GLP study was continuously monitored by Quality Assurance. The times of the inspections and the times at which the reports were forwarded to the supervisor of the laboratory and to the study director are listed below.

Inspection (Date)	Report (Date)
January 28, 1991	January 28, 1991
April 16, 1991	April 16, 1991

The results presented in the final report on this study were audited on the basis of current SOP's/analytical methods. To the best of our knowledge, they accurately represent the available raw data.

Person responsible for quality assurance:

April 16, 1991
Date

[signed]
(Willers)

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

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